BUREAU OF HYGIENE AND TROPICAL DISEASES

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# Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students; Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

## GENERAL

GRUSHKA, Theodore [M.D.] [Edited by]. **Health Services in Israel. A Ten Year Survey 1948–1958.** pp. xv+214, illustrated. 1959. Jerusalem: Ministry of Health.

Between the establishment of the State of Israel in May 1948 and the end of 1957 the Jewish population rose from 649,683 to 1,762,741. Infirmity has never been a bar to immigration, and many immigrants came from countries with low standards of life. At the same time military needs have swallowed up a high proportion of the budget, while agriculture and industry have had to be built up simultaneously with health services. The British Mandatory Government left a typical and not inefficient medical service, which however had few Jews in its senior staff and the organization of which was unsuitable for an independent State urgently engaged in pioneering, with a rapidly expanding population. Its work was supplemented by that of several voluntary Jewish medical organizations, of which Kupat Holim, the Sick Fund of the General Federation of Jewish Labour, may be taken as an example. This voluntary sickness insurance scheme was founded as long ago as 1912. It remains voluntary, though with practical Government encouragement, and at the end of 1957 had 1,200,000 members.

The predominant health problems of Israel can be divided into those accentuated by immigration, such as tuberculosis, and those naturally prevalent, malaria, schistosomiasis and primitive environmental control. The measures taken against every problem are here set forth in the matter of fact manner of an official report, supported by abundant statistics. A general chapter setting past achievements, present problems and future plans in perspective would perhaps have added to the literary interest of the report.

[A more detailed report on malaria in Israel is that of Z. SALITERNIK, *A Review of the State's Ten Years, 1948–1957*: this is reviewed in the *Trop. Dis. Bulletin*, 1960, v. 57, 102.] *B. B. Waddy*

i. NORWEGIAN FOUNDATION FOR ASSISTANCE TO UNDERDEVELOPED COUNTRIES. **The Norwegian Indian Project in Travancore-Cochin. Report No. 3. A Health Survey from the Project Area for 1953 and 1954** [LID, H. & BAASEN, Astri (Prepared by)]. 80 pp., illustrated. 1957. Oslo: Klingenberggaten 7. Norway.

ii. ——. **The Indo-Norwegian Project in Kerala (Travancore-Cochin). Report No. 4, Health Survey for 1955** [SCHREINER, C. H. & FALCK, Kirsten (Prepared by)], pp. 4–51, illustrated. **Health Survey for 1956** [SANDMO, S. & FALCK, Kirsten) (Prepared by)], pp. 52–75, illustrated. 1959. Oslo: Klingenberggaten 7, Norway.

iii. ——. **The Indo-Norwegian Project in Kerala** [SANDVEN, P., Manager]. **Health and Sanitation** (pp. 73–87). **Water Supply** (pp. 88–95). 152 pp., numerous illustrations. 1959. Oslo: Klingenberggaten 7, Norway.

i. This report describes how the project started. The Norwegian staff consisted of a doctor and a public health nurse, and Indian personnel were added. The first activity was a socio-economic survey carried out by house-to-house visits in the two villages. Special attention was paid to house structure and maintenance, sanitation, marital status and family sizes, and the incidence of tuberculosis. The information collected was put on cards, those for each house being enclosed in a folder which was kept at the Health Centre.

This report gives the findings of the survey and describes the action proposed or taken to deal with the various problems. The population of the area proved to be 10,399 of whom 42% were under 15 years of age. Housing standards were poor, 57% being huts with walls and roofs of plaited palm leaves and with a floor area of

less than 200 square feet. Most of the wells were contaminated and the underground water was of poor quality. There were only 6 public and 16 private latrines. Maternal and child welfare work was started, at first by home visiting and later at a clinic. The health problems of mothers and children are described. A survey of schoolchildren was made and an out-patient clinic for tuberculosis patients was opened. Tuberculin tests were done on schoolchildren and BCG vaccination given. Propaganda booklets on hookworm infection and tuberculosis were printed in the vernacular. Kindergarten schools already in existence were re-organized and the opportunity was taken to improve child health and to instil hygienic habits.

ii. The report for 1956 states that the Indian health authorities have taken little interest in the health work of the Project. Because of pressure of work it was recommended that an Indian doctor and an additional Indian public health nurse should be added to the staff. Home visiting was complicated by the local taboo on women going about unaccompanied. The health centre planned was erected and a children's ward was included because the parents proved incapable of carrying on their treatment.

The statistics for the period are reported and they follow the pattern of the previous report. Patients at the ante-natal clinic were examined serologically for syphilis and only 5% were found positive. The type of latrine constructed is described. The tops and bottoms were removed from 3 empty tar barrels which were placed one on top of the other sunk in the sandy soil. A concrete squatting slab was placed over the top and this was supported on a brick foundation, and it carried a concrete pan with water-seal. Short, thick bamboo pipes passed through the drums to allow escape of fluid contents. These drums were found to perish in about a year and concrete rings were substituted, each ring being separated from the next by 2 layers of bricks to permit drainage. This type is being mass-produced at an on-site cost of Rs.36.10.0. People are slow to use latrines given them, and propaganda and pressure is being used to encourage them.

Scabies is common and two teams were organized to attack the infection with benzyl benzoate on a house-to-house basis. Tuberculosis cases were treated as out-patients with streptomycin given once weekly over a long period. Anaemia is common in all age-groups and is thought to be partly due to an unsatisfactory diet composed almost exclusively of rice. The sedimentation rate was increased in 38·5% of apparently healthy adults. Plasma protein values in 42 examinations lay below normal in 43%.

The report for 1956 records the opening of a curative clinic. None of the state health officials had accepted invitations to visit the Project. The work continued on the same lines as in previous reports. The maternity ward was continually full though normal cases were only admitted if home conditions were bad. Tuberculosis continued to be a major problem; hospitalization was almost impossible and ambulatory treatment was continued, preferably with streptomycin and PAS. Routine examination of schoolchildren was started; they were given regular worm treatment and were tuberculin-tested and given BCG. Latrines have been requested by the people and 352 were built during the year; fouling of the ground was noticeably less. During the year only 48 women requested advice on birth control and many of those instructed have come back pregnant.

iii. Norwegian aid to Indian advancement began in 1952 with a project for developing coastal fisheries in a small community in the state of Kerala (formerly Travancore-Cochin). Health and sanitation were to be included in the Project and only limited personnel and equipment were permissible, because the facilities developed were to be capable of being copied by the people of surrounding areas.

The book reviewed here tells the story of the project and two of its chapters give an account of the work in health and sanitation already described in the reports reviewed above. The intention was to concentrate on preventive work, but curative work which was inescapable overwhelmed the small staff and a curative clinic had to be opened to relieve the welfare clinics. Health work consisted of clinics and home visiting by the public health nurse; tuberculin testing and vaccination against smallpox and tuberculosis was given; dried milk and other supplements to the diet were distributed and examinations made to establish local health standards. An attempt was made to raise housing standards and over 500 improved houses were built, many being of brick with a tiled roof. Latrines were given to most of the householders who had only to dig the pit and provide a superstructure. The criticism is made that the provision of free medicine encourages waste, and it is pointed out that the community is expanding rapidly and that living standards will rise only if population growth is controlled; existing methods of family limitation are not satisfactory.

In many parts of the area the water was unfit for drinking and the provision of a safe supply was undertaken. It was agreed that, instead of sinking wells, a supply should be piped in from a lake 16 miles away, which contained an ample and perennial supply at a maximum height of 9 feet above sea level. The water level will be raised 5 feet higher by building up the embankment of the lake, and the water will be pumped up the hillside to a height which would permit gravity flow to the area supplied. In order to reduce the cost of the pipe line the Foundation erected a plant for the production of prestressed concrete pipes. Though inefficiency and labour troubles reduced productivity, laying of the pipes was started in 1958. The water will be filtered and chlorinated before being piped.

It is clear that the Project has accumulated much knowledge in a short space of time and has organized an attack on many problems. *T. H. Davey*

## MATERNAL AND CHILD HEALTH

MINISTRY OF HEALTH. **Reports on Public Health and Medical Subjects No. 99. Standards of Normal Weight in Infancy.** [HENDERSON, P., Chairman]. pp. iv+35, 3 figs. [41 refs.] 1959. London: H.M. Stationery Office. [2s. 6d.]

"The standards of normal weight in infancy which are in most general use in this country are based on data of uncertain origin collected many years ago." Recent papers have shown the clear upward trend in the weights of children which has accelerated since 1945 as for example in 1 investigation in which it was found that between 1945 and 1953 the average gain in weight of boys aged 5 years in urban schools was 4·6 lb., in county schools 2·6 lb. and in London 6·3 lb.

The present survey was made in 11 localities in England and Wales:—Birmingham, Bristol, Cardiff, Kent, Leeds, Liverpool, London, Northumberland, Middlesex (Finchley), Norwich and Glamorgan (Rhondda). It was begun in all areas between the middle of 1949 and the middle of 1950. All babies, under the age of 2 months, who attended a welfare centre for the first time were enrolled in the survey provided the mother was willing. A total of 19,616 babies were enrolled but of these almost 12% were excluded from the normal healthy group for such reasons as multiple births, congenital abnormality or illness. The intention was that the survey should continue for at least 3 years during which information should be collected regularly. There were naturally many defaulters in this period and this problem is considered. The method of the survey and the information collected are fully described. These results are under the headings of representativeness of the sample, selection of normal healthy children, weight at 6-month intervals, survivors and defaulters, birth weight, attained weight to 3 years of age, association between growth and various factors, gain in weight over 4-week periods and gain in weight over 3-month periods. There is a section on the published results of enquiries made by other workers. The information is set out in 16 tables and 3 figures.

There is a long summary in which some of the findings of the survey were:—(1) the "average birth weight was 7·53 lb. for boys and 7·21 lb. for girls. Both for boys and girls the birth weight rose from first-born to later born children and for girls (at least) from the unskilled to the professional and managerial classes", (2) there are 4 phases of growth from birth to 3 years: (i) relatively variable growth for the first 4 weeks; (ii) rapid increase to 16 weeks when boys averaged about 14½ lb. and girls about 13¼ lb.; (iii) gradual slight increase in the rate of growth up to about 16 months—at 12 months attained weights were 23 lb. for boys and 21½ lb. for girls and (iv) fairly uniform growth rate thereafter until 3 years at which boys averaged 32½ lb. and girls 31½ lb. and (3) in the first few months of life smaller babies grew more rapidly than did larger babies but later the trends were reversed.

In the preface it is stated:—"We believe that the standards of normal weight in infancy obtained in the present survey and described in this Report are suitable for general use in infant welfare centres, hospitals and general paediatric practice in Britain at the present time". *M. E. Delafield*

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## CHRONIC CARDIO-RESPIRATORY DISEASES

DAWBER, W. B., KANNEL, W. B., REVOTSKIE, N., STOKES, J., KAGAN, A. & GORDON, Tavia. **Some Factors associated with the Development of Coronary Heart Disease. Six Years' Follow-Up Experience in the Framingham Study.** *Amer. J. Pub. Health.* 1959, Oct., v. 49, No. 10, 1349–56.

This paper reports the 6 years' experience of the development of coronary heart disease (CHD) in a random sample of the population of Framingham, Mass., where the National Heart Institute is conducting a longitudinal study of the development of cardiovascular disease. The sample which consisted of two-thirds of the adult population aged 29–62 years, numbered originally 6,510 persons but finally it was possible to bring in for examination 68·6% of these—2,024 men and 2,445 women. In addition a group of 740 volunteers was added to the initial group. The study covered 6 years during which period there were 4 biennial examinations. This experience is described with 8 tables of statistical information. During the 6 years there were 186 new cases of CHD composed of myocardial infarction (diagnosed by electrocardiogram and clinical evidence) 71 cases, myocardial infarction (diagnosed by electrocardiogram only) 9, sudden death in persons with previous evidence of CHD 9, sudden death without such previous evidence of CHD 18 and angina pectoris 79 cases. An analysis of this incidence of CHD was carried out in relation to (1) locality of residence in Framingham, (2) educational level, (3) national origin, (4) smoking habit and (5) alcohol consumption.

Some of the findings of the study were:—(1) the incidence of new CHD was "less at higher educational levels", (2) there was no association between national origin and the risk of CHD, (3) "Smoking was associated with an increased incidence of non-fatal myocardial infarction and of death from CHD in men 45–62. It was not associated with an increased incidence of angina pectoris". (4) "Alcohol consumption per se was not associated with CHD although heavy alcohol intake was associated with heavy smoking". *M. E. Delafield*

See also p. 104, MACGREGOR, **Fog and Health.**

## CANCER

BRITISH EMPIRE CANCER CAMPAIGN. **Thirty-Sixth Annual Report covering the Year 1958. Part II. The Scientific Report of the Researches undertaken by the Central Organisation and its Autonomous Councils in the United Kingdom, and by some of its Affiliated Organisations Overseas.** 636 pp., 1 fig. [Numerous refs.] 1959. London: 11, Grosvenor Crescent, S.W.1.

In this impressive report of scientific researches undertaken under the mantle of the British Empire Cancer Campaign covering the year 1958 there is a full list of the numerous organizations which participate and an index of the numerous research workers who are mentioned. As introduction there is a general summary of the researches under the headings of carcinogenesis; biochemistry of viruses; chemotherapy and endocrine therapy; experimental radiation studies, clinical and comparative pathology; and statistics and demography.

In the main body of the Report there are for each research centre more detailed accounts of the researches which have been carried out, with an appended list of references to work published or in the press. Scrutiny of these references, which in the aggregate number several hundreds, gives some indication of the immense amount of work which has been conducted with devotion and skill and from many scientific angles to add to our knowledge. At present many of the new facts which have come to light may have the appearance of potential fragments of a jig-saw puzzle some of which, with additions, will come together at some time and give that understanding of causation and cure which will solve the problem of cancer. *M. E. Delafield*

OETTLÉ, A. G. & HIGGINSON, J. **The Incidence of Mammary Cancer in the Bantu.** Reprinted from *Proc. II Internat. Symposium on Mammary Cancer.* Perugia, July 24–29, 1957. pp. 203–8. [10 refs.] [ ? 1959]: University of Perugia.

The incidence of mammary cancer in Bantu in the Johannesburg metropolitan area is investigated for the period 1953–55. The majority of Bantu persons attend hospital, as it is only there that treatment can be provided. Cases were picked up at the hospital.

Incidence of cancer of the male breast in the Bantu was similar to that in the American Negro. The incidence of cancer of the female breast was strikingly less than in the American Negro (49 observed in Bantu, 170·7 expected in a similar population of American Negroes). Cancer of the cervix was very common in the Bantu, a similar incidence being found to that in American Negroes (198 in Bantu, while 266·6 would be expected in American Negroes). Cancer of the body of the uterus was, however, very rare in the Bantu, only one case being found in this period, compared with 25·5 expected if the incidence had been similar to that in American Negroes. The Bantu population has a high fertility rate, and the cancer rates observed were consistent with this. *W. W. Holland*

UTTLEY, K. H. **The Cancer Death Rate in the Coloured Population of Antigua, West Indies, over the Last Seventy Years.** *Brit. J. Cancer.* 1959, June, v. 13, No. 2, 153–63. [27 refs.]

A survey of cancer mortality, based on examination of death certificates, is presented. The population examined has increased in number from 35,000 in 1887 to 55,000 in 1957. The total number of deaths attributed to cancer in this period was 1,410. The crude death rate (per 100,000) from cancer has varied from 22 in 1887–96 to 74 in 1927–36; in 1957 it was 63. Crude death rates from all causes at corresponding periods were 3,181, 1,823 and 924. Cancer mortality rate in females exceeds that in males (2:1), as has been shown for other Negro communities in the West Indies and the U.S.A.

Comparing individual sites with mortality in "white" countries it has been found that there is a relatively high proportion of cancer of the uterus (42%). Of the last 100 cases that have occurred since 1948, 39 were due to cancer of the cervix. This may be associated with a very high fertility rate (140–145 per 1,000 females aged 15–44 years) and early sexual intercourse with pregnancies in quick succession. Cancer of the breast, in contrast, is much less common than in England and Wales. Cancer of the liver was more commonly found than in England (9·4% in males, 3·0% in females of all cancer deaths), but there is no certainty that some of this was not metastatic. Cancer of the respiratory system was significantly less common and of the digestive tract more common in Antigua than in England and Wales. The carcinoma:sarcoma ratio was found to be 50:1, which is more than has previously been reported for Negro races [this *Bulletin*, 1935, v. 10, 248; 1936, v. 11, 36; *Trop. Dis. Bull.*, 1950, v. 47, 1224].

*W. W. Holland*

STABERG, Else M. Tjär- och nikotinhalt i cigarrettrök. **[Content of Tar and Nicotine in Cigarette Smoke]** *Nordisk Hyg. Tidskr.* 1959, v. 40, Nos. 5/6, 71–88, 7 figs. [14 refs.] English summary (4 lines).

At the request of the Swedish Tobacco Monopoly the National Institute of Public Health in Stockholm has carried out an investigation of the nicotine and tar content of the 19 brands of cigarettes which are on sale in Sweden; 18 foreign brands were also included in the investigation. The cigarettes were smoked in the apparatus of BRADFORD and co-workers [*Indust. & Engineering Chem.*, 1936, v. 28, 836], with a draught of 35 cc. lasting for 2 seconds, each cigarette being consumed in 8–13 draughts. The tar content per cigarette ranged from 10·4 to 31·5 mgm., and the nicotine content from 0·52 to 2·26 mgm. The results are presented in detail in figures and tables, which should be consulted in the original for further information. *D. J. Bauer*

CARRUTHERS, W. & JOHNSTONE, R. A. W. **Composition of a Paraffin Wax Fraction from Tobacco Leaf and Tobacco Smoke.** *Nature.* 1959, Oct. 10, v. 184, 1131–2. [16 refs.]

## MISCELLANEOUS DISEASES

ŠILINK, K, REISENAUER, R. & CHALOUPSKÝ, J. **The Problem of mapping Endemic Goitre in Czechoslovakia.** *Rev. Czechoslovak Med.* Prague. 1959, v. 5, No. 2, 73–88, 4 figs.

Endemic goitre exists in Czechoslovakia in some mountainous districts near the frontiers, in the central parts of the country and also in lowland areas. The gradual introduction of iodized table salt has since 1947 had good effects but has not solved the problem of goitre. Accurate methods to ascertain the extent of the endemic at any given time are therefore needed and in the present paper there is a description of a procedure which has been elaborated for this purpose.

The procedure was based on certain assumptions, one of which is "There are quantitative relationships between this average mass of the thyroid gland of the population and the intensity of goitrogenic environmental factors. The magnitude of the response, however, also depends on age and sex, and it is therefore important to compare only homogeneous groups." In 1947 the authors of this paper introduced a method for classifying degrees of thyroid enlargement by estimating the prominence of the thyroid by means of a profile line drawn from the lower portion of the surface of the thyroid cartilage to the upper edge of the sternum. There is an extensive mathematical analysis of the numerical results obtained by this method which are also compared with the actual weights of the thyroid measured in 11 Prague clinics at autopsies on some thousands of males and females over the age of 50 years. Fairly good conformity was found to exist between the weights deduced from the prominence measurements and the actual post-mortem weights provided the latter can be considered to be from a random sample of males and females over 50 years of age.

The relationship between goitrogenic intensities and geological conditions is discussed with an illustrative map of the country. Evidence by surveys of adult women in Bohemia and Moravia has shown that the "average mass of the thyroid" was "reduced as a result of iodization between 1948–1955 from 40·9 g. to 36·0 g. i.e. by 12 per cent." *M. E. Delafield*

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## MENTAL HEALTH

YAP, P. M. [M.A., M.D., M.R.C.P., D.P.M.] **Suicide in Hong Kong with special reference to Attempted Suicide.** With a foreword by Martin ROTH. pp. x + 101, 7 figs. 1958. Hong Kong: University Press. London: Oxford University Press, Amen House, E.C.4. [HK$10.00; $2.00; 12s. 6d.]

The author of this monograph has studied rates for suicide and attempted suicide in Hong Kong, using hospital and police records. In 1946 the population was just over 1,000,000; by 1955 it had almost doubled and it was estimated that a third of the residents were recent political refugees. Yap shows that the annual suicide rate rose from a low figure of 3 per 100,000 in 1946 to 12 in 1955. (This was just over the 1954 rate of 11·4 for England and Wales.)

The records for the period June 1953–December 1954 were studied in detail, yielding 263 cases of suicide and 894 attempted suicides. Many of the findings resemble those made in studies of western communities; there is a high urban rate, a smaller risk for the married, a peak rate in early summer and so on. 2 of the central arguments concern differences in age and sex specific rates and the relation between immigration and the rise in suicidal acts between 1946 and 1955.

[Although the monograph is careful and informed, many of the arguments seem based on inadequate data. For example, emphasis is placed on the steeply rising curve of suicides for those over 60, in comparison with the much lower figures (reported elsewhere) known from Chinese communities with a traditional way of life. But rates are based on small numbers: only 3% of the male population of Hong Kong is over 60, and only 10 of the 145 male suicides occurred at this age:

Many such criticisms could have fairly easily been avoided. One would have placed more confidence in the high rates for the over-60 group for example, if they had been shown to occur for another year. But the main questions arising from such studies are more general. The basic design of epidemiological and sociological research into suicide has been fairly uniform. Public records are compared with known demographic characteristics of the population, and for some groups case records may be studied in detail. Yap's survey has the merit of adding comparative data to this burgeoning field; but data gained from police and social workers' records on precipitating events can be of only limited value. Their emphasis on the effects of illness and poverty is credible enough in the light of conditions in Hong Kong today; but new ideas and methods are badly needed in this field of enquiry. At the least, research workers themselves must get nearer the original occurrences by interviewing the relatives, friends and acquaintances (and the patient himself in those who failed) near to the time of the event.] *George W. Brown*
*Margot Jefferys*

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# Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Atmospheric Pollution; Port, Ship and Aviation Hygiene; Infestation.**

## WATER AND SWIMMING BATHS

*(Including the Bacteriology of Water Supplies)*

GEHRING, A. Über die Ergebnisse 5-jähriger bakteriologischer Kontrollen in Mineralbrunnenbetrieben. **[Experience of Five Years Bacteriological Control of Mineral Water Installations]** *Arch. f. Hyg. u. Bakt.* 1959, Sept., v. 143, No. 6, 456–72. [31 refs.]

During a 5-year period in the bacteriological control of mineral water undertakings 14,240 samples were investigated. Noticeably better results were obtained than in previous investigations. Doubtless the improvements and new buildings constructed during the last few years in the majority of the concerns investigated were responsible. The questions of how coliform organisms should be assessed is discussed. Also single occurrences in individual installations were investigated and the results are included. The acid in lemonade and fruit juice drinks undoubtedly reduces the number of bacteria and the impregnation of table waters with carbon dioxide also acts to a certain extent in reducing the bacterial count. *E. Windle Taylor*

NETSCH, F. Verunreinigung des Grundwassers mit detergentienhaltigem Abwasser einer Wäscherei. **[Pollution of Ground Water by Detergent Residues from a Laundry]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebeite.* Berlin. 1959, July-Aug., v. 5, No. 4, 207–12, 4 figs.

Waste water from a laundry was led to a village pond with no outflow, and this resulted, in the course of a year, in the pollution of the well water in the surrounding district. The detergents remain unaltered in the underground water.

In the summer of 1957, when the laundry had been in action since September 1956, a change in the condition of the underground water in nearby wells was noticeable. The water began to foam in buckets on pumping, had an unpleasant taste, was refused by livestock and was finally completely unusable.

The ground water was polluted over a radius of 200 metres and it can be concluded that in the present circumstances the pollution will spread further and a number of more distant wells will be affected and become unusable. The investigation shows the detergents in waste water cannot be broken down and must therefore be considered as an important source of danger to water supplies. This is significant as they can remain unaltered in underground water for years; in fact they may even be regarded as permanent features. Therefore particular attention must be paid to the site of all new installations to see that no dangers arise.

This incident shows how important is good co-operation between all government services in the planning and erection of central washing establishments and what superior technical insight is necessary if in the future many such installations are to be relied upon in the country.

[This is a very important paper for Medical Officers of Health and Water Officials alike, being among the first examples of pollution of underground supplies by detergent residues and indicating the seriousness of this new type of pollution.] *E. Windle Taylor*

INGRAM, W. T. & MOORE, G. W. **Fluoridation in Major Cities of the United States.** *J. Amer. Water Works Ass.* 1959, Sept., v. 51, No. 9, Pt. 1, 1095–110, 2 figs.

This paper is a condensation of a report, "Water Fluoridation Practices in Major Cities of the United States", prepared for the New York State Department of Health in 1958 by the Research Division, College of Engineering of New York University. The purpose of the study was to evaluate existing fluoridation practices and make recommendations on engineering practices since questions have arisen about the feasibility of applying fluoride to large volumes of water, the persistence of fluoride ion residuals in water mains and the effectiveness of control of dosage and residuals.

20 cities which supply fluoridated water to a total population of nearly 19 million were studied, which represents about 59% of over 31 million people who were receiving fluoridated water in 1956. A very great body of information on these 20 cities is given by description, 10 tables and 2 figures. The details given are the number of the populations in the 20 cities; the capacity, average amount of water treated and method of purification used in the treatment plants; average annual water demand; characteristics of water distribution systems; water temperatures and chemical analyses of the water supplies. There are also full data on the average fluoride ion content of the waters before and after fluoridation, of the amounts of the different fluoridation chemicals which are used and the methods of their application. The costs of fluoridation are also stated and discussed. There are a number of useful observations and recommendations, based on these studies, which are of value for engineers concerned with water fluoridation.

*M. E. Delafield*

## SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

McKinney, R. E. & Symons, J. M. **Bacterial Degradation of ABS. I. Fundamental Biochemistry.** *Sewage & Indust. Wastes.* Wash. 1959, May, v. 31, No. 5, 549–56, 7 figs. [10 refs.]

Several common soil and water bacteria were isolated which would grow in pure culture in solid and liquid media with a composite blend of alkyl benzene sulphonates [ABS] as sole carbon source. The growth of some of these bacteria in a medium of glucose, nutrient broth and salts was stimulated by the addition of ABS. Having gone so far with pure cultures, the authors then switched to activated sludge for more detailed biochemical studies of the breakdown of ABS. They studied the effect on the oxygen uptake, measured in the Warburg respirometer, of activated sludge unacclimatized to synthetic sewage, of ABS and organic compounds representing the separate parts of the ABS molecule.

Up to 630 p.p.m. ABS the oxygen uptake rate was stimulated increasingly, but a concentration of 1,260 p.p.m. ABS did not produce as great a stimulation as 630 p.p.m. ABS.

At 315 p.p.m. ABS an increase in mixed liquor suspended solids from 397 to 12,700 p.p.m. produced a proportionate increase in oxygen uptake but at 25,400 p.p.m. there was hardly any further increase in this value.

[At suspended solids of over about 12,000 p.p.m. the reviewer feels that the rate of oxygen transfer from gas to liquid in the Warburg flask would become a limiting factor if air was being used in the flask.]

The shape of the oxygen uptake curves did not indicate ready utilization of ABS.

An attempt to adapt a fill-and-draw activated sludge unit to ABS as sole organic feed ended in the loss of the sludge by foaming!

Octanoate (corresponding to the hydrocarbon side-chain of ABS), toluene (corresponding to the ring structure of ABS) and p-sulphobenzoate (corresponding to the sulphonated ring of ABS) could all be metabolized by activated sludge after varying periods of acclimatization.

The metabolic block in ABS, which was not demonstrated by these authors was deduced to be a quaternary carbon atom at the junction of alkyl side chain and benzene ring in ABS. *D. Jenkins*

McKinney, R. E. & Donovan, E. J. **Bacterial Degradation of ABS. II. Complete-Mixing Activated Sludge.** *Sewage & Indust. Wastes.* Wash. 1959, June, v. 31, No. 6, 690–96, 5 figs.

In a conventional laboratory-scale (1·5 litre volume) activated sludge unit fed on a synthetic sewage and operated on a 24-hour fill-and-draw cycle, from 54 to 76% of the 10 mgm. per litre of added ABS was found to be oxidized (*i.e.* undetected by the l-methyl heptylamine method of Fairing and Short, *Anal. Chem.*, 1956, v. 28, 1827). The removal of ABS was a function of the activity of the sludge but a small amount of ABS was lost by adsorption on to the activated sludge solids.

2 complete-mixing activated sludge units (1·25-litre aeration chamber and 0·25-litre sedimentation section) were run on (1) Boston domestic sewage and (2) synthetic sewage of similar BOD.

After a period of settling down, ABS was added, the concentration being increased from 2 to 10 mgm. per litre, over a period of 48 days. The synthetic sewage-fed unit showed satisfactory performance with a 9-hour retention period and gave ABS reductions ranging from 15–80% and averaging 60%.

The domestic sewage-fed unit showed satisfactory performance on a 9-hour retention period, reducing ABS by about 60%. With a retention period of 6 hours (with suspended solids between 3,000 and 6,000 p.p.m.) the ABS reduction was between 60 and 80%, the ABS removal increasing with an increase of suspended solids.

The authors conclude that conventional activated sludge should give up to 75% reduction in ABS while complete-mixing activated sludge should give reductions in ABS of up to 80%. *D. Jenkins*

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## HOUSING

Hirsch, M. I. **African Housing in Southern Rhodesia.** *Central African J. of Med.* 1959, Aug., v. 5, No. 8, 416–23.

Owing to health requirements the habits and housing of the African have to conform to the European pattern in urban areas of Southern Rhodesia where industrialization has resulted in permanent African settlement in the towns. In 1946 an Act was passed which placed on employers and local authorities the responsibility for providing African housing to a minimum standard. In the period 1947–54 local authorities spent £4 million on African housing which was rented by employers. In 1953 a critical housing shortage occurred. Rentals had been fixed at equality for both married and single quarters so as to encourage the employment of married Africans, single rentals being used to subsidize the married ones. More married employees had been attracted and the economics of the scheme became unbalanced. House ownership offered a solution and it was believed that the African by then desired this. Money was made available for housing including one fund of £1 million to finance house-purchase. Low-cost housing in 3 areas was enthusiastically received by Africans. Payment for the home was aided by providing in it an additional room which could be let to lodgers.

During the decade ending in 1957, 50,000 single and

20,000 married units have been built in 7 towns and in addition many employees' homes have been provided by their employers. The quality of housing also has been improved. Permanent construction has replaced mud and wattle, rooms are larger, and showers, and water-borne sanitation have been supplied. Housing density is 12 to the acre and urban services of all kinds and recreational facilities have been provided. In 1958 it was further proposed that building societies should finance European-type housing up to a value of £1,500 for salaried Africans.

Many problems remain to be solved. Some areas still have a large housing deficit; overcrowding is serious in some African houses; poverty and illiteracy retard the urbanization of migrant labour. Much social research is needed for planning future accommodation; already the future married units are being modified because of increasing family size. A serious problem is that of siting African townships; central situations are too expensive for African housing and the alternative is a costly transport system requiring subsidy.

An addendum quotes very briefly the findings of the Urban African Affairs Commission. These have been rejected by the government and the alternative proposals are summarized. *T. H. Davey*

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## ATMOSPHERIC POLLUTION

SCOTT, J. A. **Fog and Atmospheric Pollution in London, Winter 1958–59.** *Med. Officer.* 1959, Oct. 16, v. 102, No. 16, 191–3, 2 figs.

In this paper there is an examination of "the trend of winter atmospheric pollution [in London] and the effects on mortality of persistent but relatively unpolluted fog and of near smog conditions". These conditions were experienced in London in the winter of 1958–9 when fog was recorded on 75 of the 182 days of the 6 months and on 3 occasions atmospheric pollution almost reached the level found in practice in London to be critical in relation to mortality.

A table gives particulars of atmospheric pollution in London in the winters from 1954–5 to 1958–9 which show that whereas the amount of "sulphur dioxide" has remained relatively constant there has been a downward trend in "smoke". Data of atmospheric pollution and temperature and of mortality during the winter of 1958–9 are given in 2 figures. The discussion leads to the conclusions: (1) "Persistent fog in November 1958 unaccompanied by high pollution had little effect on mortality", (2) the "near smogs" of January and February 1959 also appeared to have little or no effect on mortality and (3) "These events support the hypothesis that the level of pollution (in London) begins to exert a marked effect upon mortality when the daily concentration reaches 200 milligrams of black suspended matter per 100 cubic meters of air *and* 40 parts of acidic gases per 100 million parts of air, though the evidence so far does not preclude the former (smoke) being the determining factor rather than the two pollutants in combination."

*M. E. Delafield*

MACGREGOR, I. M. **Fog and Health.** *Health Bull. (Issued by the Chief M.O., Dept. of Health, Scotland.)* 1959, July, v. 17, No. 3, 60–63, 7 graphs.

"Fog and Health" was the topic of an address given at Glasgow at a joint meeting of the National Society for Clean Air (Scottish Division) and the National Industrial Fuel Efficiency Service. "Fog normally occurs in Glasgow on four or five days during each of the winter months" and in the winter of 1958–9 it was particularly severe. In this paper there is an account of the general mortality and morbidity particularly from pneumonia and other respiratory diseases (excluding tuberculosis) in Glasgow in 1958–9. These statistics are compared with those of 16 principal towns and 3 other cities in Scotland in which the general fog prevalence is less than in Glasgow. There is a description and discussion of the statistics with a number of graphs and a table which also give some particulars of records in previous years.

Among the points which emerge from this "brief study of the mortality and morbidity statistics" are that in the winter of 1958–9 a substantial increase occurred in the mortality from all causes in Glasgow which affected particularly the 65 + year age-group, and that deaths from respiratory disease "increased 9 times, while deaths from all causes were slightly more than doubled." The increase in mortality from respiratory disease in Glasgow was greater than that in the other 16 principal Scottish towns but no greater than that in Edinburgh and Dundee.

*M. E. Delafield*

# Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

## GENERAL

RÓZSAMEGYI, I. Die Rolle der Disposition bei der Entstehung der Dekompressionskrankheit [**Individual Predisposition to Decompression Sickness**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 4, 347–53.

It is a fact well known to medical officers concerned with caisson workers that a few of these suffer from decompression sickness whereas their mates remain free of any symptoms even when the circumstances of compression and decompression and the nature of the work are identical for all members of the gang.

In this paper the author mentions the conditions such as age, obesity and heart and lung defect which should debar a man from employment as a caisson worker and states that temporary ill-health may bring about proneness to decompression sickness.

The construction of the underground railway in Budapest provided statistical data for the study of the question of essential predisposition to decompression sickness. The findings of the study are described with numerical tables which set out the frequency of decompression sickness per worker in a series of periods of 6 months. In this series there was a reduction of sickness incidents per person from 1·961 in the first 6 months to 1·134 in the sixth 6-month period. This might be due to an adaptation to the conditions but the number of workers had been reduced from 691 to 127 by the end of the sixth 6-month period. When these remaining 127 workers continued for a further series of 6 periods no significant change in the number of sickness incidents occurred and these remained at a low level. It is concluded that in the first series of periods the reduction of sickness incidence was due not to adaptation but to a natural selection in that those workers who suffered frequently gave up the caisson work. In a further investigation it was found that the determination of blood pressures was of no value in indicating the existence of constitutional or temporary predisposition.

Some points of importance in the prevention of decompression sickness are described.

*M. E. Delafield*

RÜEDI, Luzius. **L'homme et son milieu. No. 2. Les traumatismes sonores de l'appareil auditif.** [Man and his Environment. No. 2. Acoustic Damage to the Hearing Apparatus] 82 pp., 43 figs. 1957. [Published also in German.] Basle 16: J. R. Geigy S.A., Switzerland.

In this monograph the author brings together much material, some of which has been published previously. He sets out the various types of acoustic trauma, and discusses these from many aspects.

The main chapters deal with hearing damage due to explosion, to detonation, to cranial contusions without fracture, and to noise. Each of these chapters is divided into sections on aetiology, symptomatology, pathological anatomy, pathology, diagnosis, prognosis, and treatment. There is a further chapter on trauma due to the noise of aircraft, while in yet another the transition between physiological fatigue and pathology of hearing is discussed.

The differentiation between explosion and detonation depends on the duration of the pressure head. If the duration is less than 1½ milliseconds the author refers to detonation, whereas if it exceeds 1½ to 2 milliseconds he refers to explosion. Charges of explosive of 20 gm. or more always produce trauma by explosion.

In the discussion of injuries due to noise account is taken of the overall intensity of sound, of the noise spectrum, the character of the noise and the duration and manner of the exposure to noise.

The many instructive figures include illustrations of histological sections, curves, and reproductions of instrumental tracings. The monograph is well arranged and should be of great interest to those who are concerned with hearing and ear injuries.

*Thomas Bedford*

CALEARO, C., FIOR, R. & PESTALOZZA, G. La sordità professionale nelle industrie dell'acciaio. Nota II. Rilievi tecnologici e clinico-statistici. [**Occupational Deafness in Steel Industries**] *Med. d. Lavoro.* 1959, June-July, v. 50, Nos. 6/7, 458–80, 8 figs. (1 on folding pl.) [Numerous refs.] English summary.

This is a statistical survey of the loss of hearing sustained by 734 steelworkers from 15 different trades of the industry, including sheet milling, boiler making, wire drawing, nail manufacture, riveting, forging, grinding, polishing and foundry work. The authors measured the characteristics of the environmental noise in intensity, range and duration and compiled a standard card for recording these findings and the history and ear, throat and nose examination, including audiometry, of each worker. The results obtained were corrected by factors to allow for the loss of hearing which normally develops with age.

Every worker had a varying degree of loss of hearing mainly to sounds of high frequency. The loss of hearing was evidently due to the environmental noises to which these workers were exposed because of their occupation. The hazard seems to be more in the

manufacture of nails, boiler making, riveting and other steel joinery, grinding and forging and to be less in foundries and sheet mills.

Previous trauma to the hearing apparatus does not seem to increase the liability to suffer from occupational deafness in the steel industry. *J. Cauchi*

NOVOTNÝ, S. & UHER, G. Beitrag zur spinalen Schädigung durch Pressluftwerkzeugarbeit (Mit dem Sektionsbefund). [**Damage to the Central Nervous System from Work with Pneumatic Tools**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 4, 339–46, 2 figs. [13 refs.]

Knowledge of the damage which may be caused by working with pneumatic tools is relatively recent, nevertheless many observations on this subject have been recorded. In this paper there is a review of the literature which has dealt mainly with injury to joints and the vasomotor system [this *Bulletin*, 1945, v. 20, 480; 1948, v. 23, 114; 1955, v. 30, 516, 986]. Damage to the nervous system has been described but attention has been focussed on the peripheral nervous system and only occasional observations of involvement of the central nervous system have been reported.

There are 2 case reports of such involvement in workers in the authors' own experience. The first patient was a pneumatic drill worker in whom atrophy of the hand muscles developed, with gradual extension of muscular weakness to the shoulder and then the lower limb muscles. The clinical diagnosis was progressive muscular atrophy of central nervous origin caused by his work. The second case was in a man aged 67 who had worked for a considerable number of years with pneumatic tools. His illness began with weakness in the left hand (he was left-handed) which later extended to the right hand and the shoulders. Examination showed muscular wasting of the hands with clawing of the fingers, fibrillation of muscles, sluggish or absent reflexes in the upper and lower extremities with disturbed sensation. X-ray examination of the spine revealed marked spondylitis. After 4 years during which his condition deteriorated he died suddenly of heart failure. There is a detailed description of the macroscopic and microscopic findings post mortem which were extensive degenerative changes in the brain, spinal cord, peripheral nerves and muscles. These 2 cases and a few other similar recorded cases are discussed clinically. *M. E. Delafield*

BRIEGER, H. & LABELLE, C. W. **The Fate of Inhaled Particulates in the Early Postexposure Period.** *Arch. Indust. Health.* Chicago. 1959, May, v. 19, No. 5, 510–15, 4 figs. [16 refs.]

Rats were exposed for 7 hours to aerosols of an insoluable green dye formed by spraying aqueous suspensions. The airborne concentration of dye was near to 20 mgm./m.$^3$ and the aerosols are described as 2 micron or 6 micron without stating whether this is radius or diameter or how the actual sizes were spread about the nominal figures.

The animals were killed at periods up to 334 hours after the start of the exposure and the amounts of dye were estimated (a) in the lungs together with the trachea and tracheobronchial lymph nodes, (b) on the skin, (c) in the gastro-intestinal tract and its contents.

The results of the experiment are displayed by tables, graphs and diagrams, each entry in the tables being the mean of about 15 experiments with 20–30% standard deviation.

For both the 2-micron and 6-micron clouds the contents of each organ (a–c) increased during exposure and decreased after exposure had ceased. The maximal recoveries, which therefore occurred at 7 hours, expressed in mgm. per kgm. body weight were:

for 2-micron aerosol—(a) lungs etc., 0·714, (b) skin, 26·246, (c) G-I tract, 4·989;

for 6-micron aerosol—(a) 0·7, (b) 7·45, (c) 4·172.

Recovery in the faeces, which were collected at 24-hour intervals after exposure to the 6-micron aerosol, rose to about 7 mgm./kgm. body weight at 72 hours and then remained constant to 168 hours.

With each aerosol the rate of clearance from the lungs was much slower than from the other organs, especially for the 2-micron cloud, and towards the end of the experiments the rate was very small indeed.

There was thus a change in the proportion of dye in the different organs after the termination of exposure. During exposure the greatest amount was on the skin and the least in the lungs. One day after exposure to the 2-micron cloud the greatest amount was found in the gastrointestinal tract. One week after exposure the highest proportion was in the lungs and the lowest on the skin in each case. The clearance of 2-micron particles from the lungs took place with a "half-life" six times longer than the 6-micron.

The significance of the intestinal burden is thus seen to be greatest a few days after exposure, while the lung burden dominates the picture after a week or so.

*C. N. Davies*

## OCCUPATIONAL PHYSIOLOGY

GRÜN, L. & STROHMENGER, P. Untersuchungen über die Gefährdung der Gesundheit des Hitzearbeiters. [**Health Dangers of Work at High Temperatures**] *Arch. f. Hyg. u. Bakt.* 1958, June, v. 142, No. 4, 276–87, 1 fig. [16 refs.]

In this paper there is mention of some of the work that has been done on the health of workers in high temperatures and a short description of the physics of the heat radiation in certain industries. The investigation which is here described concerned 663 workers at a steel works. These men were composed of 3 groups:—(1) 231 shift workers who were exposed to high levels of heat radiation, (2) 185 men not exposed to such heat but engaged in heavy work, and (3) 247 men not exposed to heat and engaged in light physical work.

The health status of these 3 groups was assessed by reference to sickness records in respect of (1) feverish infections such as colds, tonsilitis, pharyngitis and influenzal conditions, (2) pneumonia and pleurisy, (3) chronic bronchitis and (4) rheumatic pains entitled Rheuma. These sickness data were examined with the result that no real statistically significant difference was found between the 3 groups of workers in their experience of the feverish infections and the respiratory conditions. Rheumatic pains, however, were found to be more prevalent in both of the 2 groups of men who carried out hard work than in group 3 composed of men doing light work. The general finding of this investigation is that exposure to heat radiation does not predispose workers to the disease states which were considered. *M. E. Delafield*

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Communication No. 156. Problèmes médicaux soulevés par le travail aux températures élevées. 5e partie. Entrainement de sauveteurs à des températures sèches supérieures à 45°C. avec une humidité relative voisine de 50%. [**Medical Problems Arising from Work at High Temperatures. Part 5. Training of Rescue Workers at Dry-Bulb Temperatures above 45°C. with a Relative Humidity of about 50%**] [LEYH, P.]. 1958, Oct. 15, v. 13, No 7, 45 mimeographed pp. [16 refs.]

The training of mines rescue workers, previously acclimatized to work at high temperatures, is carried out at the Centrale de Sauvetage du Borinage at a dry-bulb temperature of 43°C. (109·4°F.) and a wet-bulb temperature of 30°C. (86°F.), and earlier reports in this series [this *Bulletin*, 1955, v. 30, 771; 1958, v. 33, 492] have described studies of the physiological reactions produced by work at these temperatures.

At times of mining accidents, and especially when fires or explosions occur, rescue teams are called upon to work at temperatures distinctly higher than those just mentioned. Further experiments have therefore been carried out on acclimatized subjects at dry-bulb temperatures of 46° to 47·5°C. (114·8° to 117·5°F.) with wet-bulb temperatures of 35° to 37°C. (95° to 98·6°F.), *i.e.*, with a relative humidity of about 50%.

2 types of exercise were used. In 1 series of experiments the men exercised for 70 minutes at the temperature of 46°C. During that time they walked at a speed of 4 km./hour for 20 minutes, then for 12 minutes, in the middle of which period a rest of 1 minute was taken; during the 12 minutes they simulated a type of rescue operation by moving blocks of concrete each weighing 30 kgm., each man moving at least 50 blocks. There followed a rest for 10 minutes (still in the hot chamber), and then walking was resumed for the remainder of the 70 minutes. In the second series of experiments the men were exposed to the more severe conditions of 47·5°C. dry-bulb temperature and 37°C. wet-bulb for a period of one hour, during which time they walked at 4 km./hour, with a rest of 10 minutes in the middle of the hour.

Detailed results of the experiments are given in the paper. From the results it is concluded that men trained to work in an environment of 43°C. dry-bulb and 30°C. wet-bulb temperature can straight away perform the moderate work of walking on the level for a period of 1 hour at temperatures of 47·5°C. dry bulb and 37°C. wet bulb, without any marked subjective difficulty. On the other hand, harder work, even of short duration, is often less well tolerated, and may provoke disagreeable symptoms and even loss of consciousness.

It is also concluded that on the basis of prior tests in severe environments it is possible to make some selection among rescue workers, and thus to employ the more heat-resistant men in the conditions of greatest heat. *Thomas Bedford*

HOSEY, A. D. & MENDENHALL, A. C., Jr., **The Envirecan Instrument for Continuous Recordings of Environmental Air, Wet-Bulb, and Globe Temperatures, and Air Velocity.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 121–30, 10 figs.

The 4 factors which make up the thermal environment are the temperature, humidity and speed of movement of the air and the radiation from the surroundings. If the environment is to be completely specified all these 4 factors must be taken into account. The radiation flux at a point, commonly given in terms of the mean radiant temperature, can be estimated from readings of the globe thermometer if the temperature and speed of the air are also known. In this paper the authors describe an instrument which records on 1 chart the 3 atmospheric variables and the globe temperature.

The instrument consists of 4 sensing or detecting circuits and a system for recording the output signal from each circuit successively and repetitively. The sensing unit for air speed consists of a thermistor-bridge circuit in which the cooling effect of air circulating over a heated thermistor is used as an indicator of the air speed. The dry-bulb, wet-bulb and globe temperature units consist of thermistor-bridge circuits. For the measurement of wet-bulb temperature an oral thermistor-thermometer probe covered with a sling psychrometer wick is used, the wick being connected to a small bottle of water by means of rubber tubing. The thermistor bead in the globe thermometer circuit is blackened and is mounted at the centre of a 5-inch copper toilet float which is coated inside and outside with dull black enamel. The construction of the instrument and the electrical circuits are described and illustrated. The methods of calibration are also described and calibration curves are reproduced.

The instrument has been used for the study of industrial heat exposures, and from the experience thus gained it is thought that some modifications are desirable. However, the instrument promises to be of much value. It appears to give results of considerable accuracy, and it records for prolonged periods. It is a most interesting development. *Thomas Bedford*

## OCCUPATIONAL DISEASES

ROACH, S. A. **Measuring Dust Exposures with the Thermal Precipitator in Collieries and Foundries.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 104–22, 13 figs. [53 refs.]

Two surveys, one in a colliery and the other in a steel foundry, are described to illustrate the differences in the techniques adopted and the results obtained.

For surveys of airborne dust in coalmines the thermal precipitator has been modified to make it more portable and less liable to damage. In the modified apparatus a cap-lamp battery with an ammeter, switch and rheostat incorporated in the top cover plate is used, and a small reversible aspirator replaces the can of water, jet and measuring cylinder used in the standard apparatus. The total weight of the modified equipment is 10 lb., compared with 24 lb. for the standard equipment.

A microprojector is used for assessing the dust samples, and the arrangement of the projector is described in the paper. With coalmine dusts only particles of 0·5–5 microns diameter are counted. In other industries in connexion with which little is known about the nature and size distribution of the dust a full count and size distribution will help to assess the probable hazard and often to identify the source of the pollution.

In an industrial environment, as in a coalmine, dust concentrations vary considerably, from time to time in the same place, owing to changes in the work being done, and from place to place. In a series of observations the variability is liable to correspond with a standard deviation of about 50% of the average concentration. Part of this variability is due to errors of sampling, but a more important source of error is a bias due to overlapping among the particles collected on the cover glasses, especially when the deposit is dense.

The product of the average concentration of dust and the duration of exposure is probably a good index of the dose of dust retained in the lungs. The duration of exposure is measured by a simple time study made at the same time as the concentration of dust is being measured. Samples are taken near workers chosen at random. Ideally successive samples are taken alongside different workers, but in the colliery survey which is described it was not possible to do this, and each day had to be spent with one collier. In this survey the mean dust exposures were 2,860 particle-hours per shift for coal-getters, 2,250 particle-hours for those on stone work, and 1,010 particle-hours for the other workers.

During the survey in a steel works successive samples could be taken alongside different workers. The dust concentrations seemed to be unrelated to the apparently dusty processes, and as the dust was very fine it was suspected that it was the normal atmospheric pollution of the neighbourhood. This was confirmed by samples taken outside.

Dust surveys such as those described in the paper cannot be made cheaply, for the cost is found to lie between £1 and £2 per sample taken. Consequently, alternative instruments which can be run for long periods unattended are being developed.

If in future researches respiratory ventilation and dust exposures are both measured, those measurements combined with the results of periodic medical examinations would enable the relation between dust exposure and its effect on man to be determined. *Thomas Bedford*

HARTMANN, W. L Untersuchungen über die Vergliechbarkeit der Resultate verschiedener Staubmessmethoden. **[A Comparison of Certain Dust Sampling Methods]** *Staub. Düsseldorf.* 1959, Oct. 1, v. 19, No. 10, 345–51, 3 figs.

The results obtained with several sampling devices were compared by visual microscopic counting, with phase contrast illumination which is stated to be particularly beneficial for specimens of quartz dust. A preliminary test of the 5 persons who made the counts was carried out on 10 thermal precipitator samples and revealed individual scatter of 6·0 to 12·55% and errors of the mean from 1·0 to 4·0%.

Comparison of British and Italian thermal precipitators in a ceramic factory gave counts agreeing within a range of 1·3 to 15·2% for individual pairs of samples and within 1·5% for the group average.

With quartz dust dispersed free from aggregates with a Wright dust-feed mechanism in a 15 $m^3$ chamber, a comparison of a midget impinger with a thermal precipitator revealed good correlation. Thermal precipitator counts over the size range 0·3 to 5 microns exceeded the impinger counts by a factor of more than 3, but t.p. counts from 1 to 5 microns were only about 75% as large since the impinger did not retain the finer particles.

French Le Bouchet filters, assessed gravimetrically, did not correlate well with the concentration by number of particles. This is ascribed to the predominant effect of a few large particles upon the filter data.

Higher dust concentrations were dispersed with the feed mechanism by increasing the air flow and releasing the dust through an impinger which stopped aggregates of particles from escaping. Samples were then taken with the filter, a thermal precipitator and a sedimentation cell. The filter samples were washed off and graded in a Gessner micro-sedimentation apparatus; the resulting weight distribution was used to calculate the number concentration for comparison with the thermal precipitator and sedimentation counts. The average of 5 filters gave 16·2 mgm./$m^3$ and 1,845 particles (1–5 microns) per $cm^3$ compared with 1,778 from the thermal precipitator.

Number comparison between thermal precipitator and sedimentation cell (0·2–5 microns) made the latter appear 5% higher.

[It is conceivable that the small deficiency in the thermal precipitator results may be due to overlap error which is neglected.]

Further experiments in factories, in which the filter and the thermal precipitator were compared over the range 1–5 microns and the filter weights were converted to numbers by sedimentation analysis, as above, resulted in the counts estimated from the filter samples being consistently high, often by a considerable factor. This is put down to the presence of aggregates which are broken up in liquid suspension.

With the standard French soluble filter and counts only of particles below 3 microns good agreement was found with the thermal precipitator counts in the range 0·5 to 3 microns. *C. N. Davies*

QUINOT, E. & KUEFFER, D. Sur le choix d'un depoussiéreur adapté aux chantiers miniers. Exemple de réalisation. [**Choosing a Dust Remover for Use in Mines. A Suitable Design**] *Rev. Méd. Minière.* Sin-le-Noble. 1959, v. 12, No. 40, 43–59, 9 figs. [20 refs.]

In spite of all precautions against the spread of dust from sources of emission, an appreciable number of particles invariably escape to contaminate the general ventilating air of a mine. It is difficult to remove them on account of the large volume of air and the low dust concentration.

To arrive at an engineering specification for a dust remover capable of performing this task the authors assume the size-distribution of the particles to be given by the formula of WYNN and DAWES (*Safety in Mines Research Establishment Research Report* No. 28, 1951) for coal dust with neglect of the $\beta$ term which represents mainly pollution in the downcast air.

Arguing that the danger of silicosis from breathing dusty air must be related either to the total surface area or to the total mass of the dust deposited in the alveoli of the lungs, the authors quote the surface area and mass distribution formulae which peak at the values $2/\alpha$ and $3/\alpha$, respectively.

Taking $\alpha=0{\cdot}44$ for coal dust, this puts the most frequent surface area at 4·5 microns diameter and the most frequent mass at 6·8. For rock dust $\alpha$ is taken as unity, making the corresponding maxima fall at 2 and 3 microns.

It is then claimed that the elimination of all particles exceeding 2 or 3 microns would do away with more than 80% of the danger of breathing the dusty air.

Having written down the specifications of the performance of the dust extractor an examination is made of the different basic mechanisms by which it might operate. This leads to the conclusion that the only practical system must involve the collision of dust particles with liquid droplets, in which they became incorporated, followed by inertia deposition in a rotating fan.

Implementation of this conception comprises a coaxial jet water-spray which acts, also, as an ejector entraining the main air input. The water droplets and dusty air pass through a venturi where collisions between particles and droplets ensue owing to turbulence. The effluent proceeds axially into a rotating fan to the blades of which are attached stainless steel wires; the droplets impinge on these. The aqueous suspension is then flung outwards to the enclosure of the fan from which it drains away.

The apparatus consumed 1·5 $m^3$/minute of compressed air and entrained 1·3 $m^3$/second of dusty air.

[While this attempt to rationalize the design of a dust extractor must be applauded, certain weaknesses in the argument exist.

Silicosis and coal dust pneumoconiosis are different diseases and there is little justification for relating the incidence of either to the total surface area or mass of dust particles between 0·5 and 10 microns diameter. Either disease could be caused by the inhalation of particles smaller than 2 or 3 microns. The validity of the distribution for silica dust might be questioned and in any case it is illogical to use the distribution formula for airborne dust to establish the instrumental efficiency. This formula requires to be modified by the alveolar deposition formula, which is known roughly, if not by the alveolar retention expression which is commonly taken to be the same as the deposition one. The effect of correcting the airborne size distribution for alveolar deposition would be to increase the importance of smaller particles so that the extraction would really be less efficient than is supposed.

The extractor will collect particles greater than 10 microns, of which the size distribution formula takes no account, so that an exaggerated idea of its efficiency might arise in this way also.] *C. N. Davies*

HOPWOOD, B. E. C. **A Study of the Health of a Group of Miners in the South West of Uganda.** *Trans. Ass. Indust, Med. Officers.* 1959, July, v. 9, No. 2, 69–75.

There has been little industrial development in tropical Africa, and consequently little has been published about the health of workers there. Mining is one of the oldest established industries, and this paper presents the results of a small survey in a group of mines in south-west Uganda.

There were 5 mines, 2 opencast and 3 underground; wolfram was worked in 4 and tin in 1. Only 1 had been in operation for more than 14 years, and since wet drilling was introduced generally in 1943 this was the only mine in which dry drilling had been carried on.

The average total number of workers was 1,235, the total number interviewed was 314 and the number examined 270. The average age was 28·5 years (16 to over 50).

In nearly all cases mining was carried out at a comparatively short distance from the surface so that conditions were not as bad as might be supposed.

Dust counts, which could not be assessed reliably, indicated that in all cases they rose in the vicinity of the machines. There were examples of a dust content of 13% in some places in spite of wet drilling. In one of the opencast mines there was a high content of quartz dust but this was in the open air and only once a week.

The majority of the workers were from the locality, and there was little dependence on imported labour. The mining occupations are listed in detail; the majority of the workers had worked underground or been otherwise exposed to dust. The average time they had been employed was 54 months.

Enquiry about past health and admission to hospital showed that about 60% of their past ill health was related to chest symptoms.

There were no facilities for X-ray examination but it was the impression from a simple physical examination that silicosis is not yet a disease of importance in the group. There was a high incidence of minor respiratory disorders (23% compared with 3% in a similar group of cement workers), probably not connected with occupation. *H. G. Calwell*

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Communication No. 162. Recherches antomiques sur la topographie des confluences pneumoconiotiques. 2e partie. Localisation des confluences pneumoconiotiques. [**Anatomical Researches on the Topography of Massive Pneumoconiosis. Part. 2. Distribution of Areas of Massive Fibrosis in Pneumoconiosis**] [MEERSSEMAN, F., BELAYEW, D. & MINETTE, A.] 1959, July 15, v. 14, No. 5, 44 mimeographed pp., 31 figs. [13 refs.]

The object of this study was to define and plot the anatomical sites of areas of massive fibrosis in pneumoconiosis. Lungs were injected with a solution of gelatin differently coloured for each separate lung segment [this *Bulletin*, 1957, v. 32, 1064]. They were then cut sagittally. In this way 21 right lungs and 24 left lungs obtained from 29 necropsies in Belgian coalminers were examined [the lungs unaccounted for were discarded because of damage]. The site of the masses was charted as illustrated diagrammatically in the text. Frequency of involvement of individual lobes and segments is tabulated.

Among the more important conclusions are that the fibrotic masses tend to involve the upper and middle zones of the lungs, especially posteriorly, and as a rule the lungs are affected more or less symmetrically. In the majority of cases the mass is not confined to a single segment but invades several.

The findings differ from those of other research workers but the explanation may be that coal, quartz and other dusts produce different patterns of distribution of fibrotic masses. *A. Meiklejohn*

PERNIS, B., CLERICI, E. & GHEZZI, I. Studio immunologico delle proteine del siero di sangue adsorbite sulla silice cristallina. [**Immunological Study of Serum Proteins adsorbed on Crystalline Silica**]. *Med. d. Lavoro.* 1959, June–July, v. 50, Nos. 6/7, 405–11, 3 figs. [21 refs.] English summary (5 lines).

Using immunological methods, the authors of this paper set out to investigate (1) the possible changes in the antigenic structure of gamma globulins when these have been adsorbed on quartz and (2) the exact nature of the proteins which are adsorbed on a small quantity of quartz which has been left in contact with an excess of whole blood serum. For (1) pure human gamma globulins were first adsorbed on quartz powder and then tested for antigenic properties against gamma-globulin antiserum. The quartz in (2) was treated with an excess of fresh human serum and then tested against a serum which contained antibodies for the various protein fractions of human serum to determine which of these protein fractions had remained fixed on the quartz.

They describe the ingenious technique, devised by OUCHTERLONY, which they followed, and give photographic reproductions of the patterns obtained on agar plates, as a result of gel diffusion and immunoprecipitation.

It was found that gamma globulins adsorbed on quartz dust retain their specific antigenic properties and that the immunological reactions in cases of silicosis are not due to the formation of antibodies against the patient's own serum proteins altered by their adsorption on quartz, as believed by SCHEEL *et al.* [this *Bulletin*, 1954, v. 29, 634].

It is suggested that in silicosis the endothelial cells which have ingested particles of quartz die and the resulting cytolysis sets free antigenic substances which provoke the formation of, and react with, antibodies to activate the processes of fibrosis. *J. Cauchi*

PERNIS, B., MAGISTRETTI, M. & BOLIS, L. Variazioni nella resistenza alle endotossine in topi trattati con tridimite per via endovenosa. [**Variations in resistance to Endotoxins in Mice Treated Intravenously with Tridymite**] *Med. d. Lavoro.* 1959, June-July, v. 50, Nos. 6/7, 412–16. English summary (8 lines).

Like quartz, tridymite consists of silica and the authors have used 2 different preparations of this mineral and one lot of prepared quartz for the laboratory experiments which they report in this paper. The granules were less than 1 $\mu$ in 70% of one tridymite, 90% of the other and 76% of the quartz. The mice used were Swiss Rockland breed weighing 20 $\pm$ 1 gm. and the animals were each given one intravenous injection of 5 mgm. of the silica powder suspended in 1 cc. of normal saline. The powder finds its way to the liver and in a lesser degree to the spleen and these organs react with a proliferation of phagocytic macrophages and plasma cells. A proportion of the mice succumbed to the injection within a week.

The survivors were tested for sensitivity against O antigen of *Salmonella typhi* which was injected intraperitoneally 7, 15 and 30 days after the tridymite treatment in doses of 4, 40, 130, 400 and 1,000 $\mu$gm. respectively. For each experiment the mice were divided into 5 groups of 7 each and antigen (the "endotoxin" of the experiment) was also injected into controls which had received no tridymite.

It was found that the resistance of the mice to endotoxin was lowered as a result of the previous treatment with silica. As with certain chronic infections from BCG [this *Bulletin*, 1959, v. 34, 279] and other live bacteria, the lowered resistance to endotoxin may be due to endogenous endotoxin-like substances which are set free as a result of the damage of the macrophages due to the silica. *J. Cauchi*

GHISLANDI, E. Chemio-terapia della silicotubercolosi: esperienze con pirazinamide e cicloserina. [**The Chemotherapy of Silicotuberculosis: Experiences with Pyrazinamide and Cycloserine**] *Med. d. Lavoro.* 1959. June–July, v. 50, Nos. 6/7, 417–25. [20 refs.] English summary.

Ghislandi discusses the problem of treating cases of silico-tuberculosis after they have shown a resistance to such proved remedies as PAS, streptomycin and isoniazid. He reports 18 cases, 15 of which had developed clinical evidence of bacterial resistance to 1, or to a combination, of these "major" antibiotic and chemotherapeutic agents. 9 of the patients were given pyrazinamide and 9 others cycloserine, and these "minor" antibiotic and chemotherapeutic agents were combined with the administration of isoniazid in 16 patients. The

majority improved, some were arrested but 1 got worse. Of the 3 patients who had not previously undergone specific treatment, 2 did well on pyrazinamide and 1 on cycloserine. Pyrazinamide caused toxic jaundice in 1 patient, but this passed off and the patient improved and became sputum-negative in due course.

In this small series, cycloserine seemed to act more effectively on the specific chest lesion while pyrazinamide rendered the sputum negative in a shorter time. The former is less toxic and is easier to handle than the latter. *J. Cauchi*

GHISLANDI, E. & FINULLI, M. Su due casi di silicosi massiva associata a neoplasia polmonare. [**Two Cases of Massive Silicosis associated with Pulmonary Tumours**] *Med. d. Lavoro.* 1959, June–July, v. 50, Nos. 6/7, 426–31. [28 refs.] English summary.

Ghislandi and Finulli refer to the "immunity" theory which VIGLIANI and PERNIS have recently developed to explain the progressive massive fibrosis of pneumoconiosis [see this *Bulletin*, 1959, v. 34, 347]. When inhaled, quartz is ingested by the endothelial cells of the lung, these cells are damaged and certain lipo-polysaccharides are set free; these autogenous "endotoxins" act as antigens, provoke the formation of antibodies and react with these to precipitate serum globulin which leads to hyaline deposits. In the pathogenesis of massive fibrosis, there has been propounded the existence of a contributory factor, such as tuberculous infection, acting in association with the silica to activate this antigen/antibody production.

From their clinic in Milan, the authors quote the post-mortem records of 39 cases of massive fibrosis in only 18 (46·2%) of which they found tuberculous disease to be associated. They assume that other, non-specific, infections of the broncho-pulmonary system and, indeed, other diseases of the connective tissues such as chronic primary polyarthritis and scleroderma may serve as the necessary contributory factor to the massive fibrosis in silicosis.

The authors describe 2 cases where there was both massive fibrosis and cancer and suggest a relationship between the two processes. The carcinomatosis may have set free endotoxic bodies of a lipo-polysaccharide nature with antigenic properties capable of activating immunity reactions provoked by the quartz.

*J. Cauchi*

AHLMARK, A., BRUCE, T. & NYSTRÖM, Å. Om progresstendensen vid silikos. [**On the Progressive Tendency of Silicosis**] *Nordisk Hyg. Tidskr.* 1959, v. 40, Nos. 9/10, 203–9, 1 fig.

The English summary appended to the paper is as follows:—

"The progressive tendency of pneumoconiosis in quartz workers, steel fettlers, pottery forming-shop workers, drillers in iron ore and moulders of pig iron was investigated on the basis of cases notified to insurance boards. Progression was on the whole independent of whether or not the dusty work was discontinued when pneumoconiosis was diagnosed. In quartz workers and steel fettlers, stages I and II of the disease frequently became worse within as little as 5 years, and in pottery workers within 10 years. In iron-ore drillers and iron moulders, pneumoconiosis showed much less progressive tendency; after as long as 15 years the same stage was present in most cases."

PITZURRA, M. & SALAMANDRA, R. La silico-tuberculosi nelle miniere del Grossetano dal 1954 al 1957 [**Silico-Tuberculosis in the Grossetano Mines, 1954–57**] *Lotta c. la Tubercolosi.* 1959, June, v. 29, No. 6, 773–81. [13 refs.]

Iron pyrites (nearly 83% of the whole output from Italy—792,467 tons in the first quarter of 1958), mercury, antimony, iron and lignite are all mined in the Province of Grosseto, near Perugia, and well over 5,000 miners are employed, working at depths which vary from 250 to 400 metres. The ventilating and drying systems are up-to-date, wet methods are used for drilling, to keep down dust, and the miners are issued with masks, but they tend to neglect these protective measures in endeavouring to achieve increased production which earns bonuses. Silicosis is quite prevalent among pyrites miners and in many cases the disease has been contracted before all the modern safety measures had become available.

The authors of this paper have been engaged in the laboratory investigation for the diagnosis of tuberculosis in these pyrites miners since 1954, carrying out the Mantoux test, differential and other blood counts, haemoglobin estimation and culture of the sputum for the tubercle bacillus. Where culture was positive the duration of employment has been examined and the exact kind of work done, and they assessed the working efficiency of the affected workmen. In fatal cases they studied the morbid anatomy and they now report their findings.

Data are tabulated in full detail for all those found culture-positive in the 4 years 1954–57. 933 miners were examined and 271 (29·58%) were found to have silicosis; 71 (25·63% of the silicotics) had tuberculosis and 16 of these had died by the end of 1957. Some had developed silicosis with tuberculosis by the 5th to 9th year of mining.

The authors report other details from their investigation such as age incidence and percentage loss of working efficiency. *J. Cauchi*

PINO, G. Aspetti clinici e funzionali della silico-tubercolosi. [**Clinical and Functional Aspects of Silico-tuberculosis**] *Lotta c. la Tubercolosi.* 1959, June, v. 29, No. 6, 782–94, 6 figs. [23 refs.]

Pino quotes the literature showing that tuberculous infection complicates more cases of silicosis than are usually diagnosed during life by using clinical methods and X-rays. Regularly repeated examination of persons at risk has shown that as short an exposure to the hazard as 6 months may cause the appearance of silicosis, fatal in some cases, many years later: it is obvious how the diagnosis may be missed in the absence of a history of recent exposure to the risk.

Without tuberculosis, cavities may still form in the

lungs of silicotic patients, due to fibrosis, ischaemia and consequent tissue necrosis. Clinical and X-ray examination is not enough, laboratory investigations must be undertaken in addition to confirm the diagnosis of tuberculosis in cases of silicosis. A combination of raised sedimentation rate, a strong Mantoux-positive reaction and certain characteristic changes in the serum proteins may justify a diagnosis of tuberculosis with silicosis even when the specific organism itself has not been identified morphologically.

Because of its action on the bronchi—irritant and inflammatory—silica dust can be shown to have already impaired the functional efficiency of the lungs even before it has reached the alveoli. Pino discusses a number of functional tests, illustrating them with case-reports, and then deals with the treatment problem. Removal from exposure to the hazard, even at the first signs and symptoms of silicotic involvement, may fail to arrest the disease. Antibiotic treatment may cause the disappearance of the bacilli from the sputum, and even result in an improvement of the general condition, without appreciably affecting the progress of the disease.

*J. Cauchi*

MIKLÓS, T. A fapor, karborund és korund müköporok kórtani je legzetességei. [**The Pathological Characteristics of Wood-Dust, Carborundum and Corundum Artificial Grinding Stone Dust**] *Munkavédelem.* Budapest. 1959, v. 5, Nos. 1/3, 29–32. [11 refs.] English summary.

An investigation has been made of the pathological effects produced by the inhalation of certain dusts. The intratracheal administration of 50 mgm. of beech wood dust in rats produced a foreign body reaction in the lungs. 38 men who had been exposed to beech dust in a joinery shop for up to 40 years were examined radiographically, and in 12 the lungs showed slight to extensive nodular opacities which were not correlated with time of exposure. In 6 instances polarographic determinations on the serum gave values deviating from the normal. There was no reduction of working capacity. Rats were given 70 mgm. of finely ground carborundum or corundum intratracheally; in histological examinations of the lungs carried out 1–3 months later there was no evidence of progressive fibrosis, and no pathological changes apart from a minimal foreign body reaction. In radiological examinations carried out on 52 workmen who had been engaged in grinding or polishing metal with carborundum for 1–8 years 46 showed no abnormalities in the lungs, 2 showed grade 0–I and 4 grade I silicosis.

*D. J. Bauer*

TROISI, F. M. Sul rischio pneumoconiotico da polveri di cereali in scaricatori portuali. [**The Pneumoconiosis Danger from Corn Dusts in Dockers**] *Rass. Med. Indust.* Rome. 1959, Mar.–Apr., v. 28, No. 2, 89–102 [36 refs.] English summary.

30 dock workers who worked at unloading grain were examined for possible dust disease. None had been exposed for more than 5 years or less than 6 months. Although unloading was mostly mechanical, by suction into the silos, some handling had to be done and the men were especially exposed to risk when cleaning up holds after bulk transport or when sacking the grain. Almost immediately after beginning such work newcomers had some constitutional disturbance with fever and symptoms of irritation of the upper air passages; nearly all those who had done such work for more than 3 years had moderate bronchial catarrh, sometimes with asthmatic attacks. Chest skiagrams showed increased lung markings, parenchymatous "marbling", moderate emphysema, and slight micronodulation. In 23 patients *Candida albicans* was found in the sputum [but also in 10 controls]. Examination of the dust from 2 sites gave 6·32% and 8·33% free silica; the particle sizes were mostly above 10 $\mu$.

The author thinks that it can be accepted that the changes in the respiratory apparatus shown clinically and by X-ray examination must be related to the inhalation of grain dust. He makes some comments on prevention and considers that the proper medical selection of the workers is of fundamental importance.

*W. K. Dunscombe*

CREMER, Jill E. **Biochemical Studies on the Toxicity of Tetraethyl Lead and Other Organo-Lead Compounds.** *Brit. J. Indust. Med.* 1959, July, v. 16, No. 3, 191–9, 1 fig. [28 refs.]

The toxic action mechanism of tetraethyl lead on brain metabolism in rats was studied by investigating the effects of tetra-, tri- and diethyl lead and lead acetate *in vivo* and *in vitro* on brain slices and brain brei [pulp] preparations. Comparisons with organic tin compounds are noted. A method using dithizone, which measures tri- and diethyl lead as intact monovalent organo-lead ions, made it possible to demonstrate that fat-soluble tetraethyl lead is broken down in the liver to the more toxic water-soluble triethyl lead which is responsible for the toxic effects. It remains stable for at least 4 days and any subsequent degradation to the less toxic diethyl lead or to inorganic lead takes place more slowly. The effect on brain metabolism appears to be due to the organic lead composition and not primarily to the lead content.

Tetraethyl lead intravenously or triethyl lead chloride intraperitoneally resulted in identical signs of poisoning. Though the lethal dose necessary was greater with the former the amount of triethyl lead in the brain was similar in both groups. The concentration in the brain was not high in comparison with that in other tissues but brain tissues appear sensitive. Metabolism was altered in slices from both groups, and inhibition was identical with that of slices to which triethyl lead was added *in vitro*.

*In vitro* studies showed a difference between the actions of the 4 compounds. Tetraethyl lead and lead acetate had no effect. The action of diethyl lead was prevented by the addition of BAL or thioglycollic acid. Triethyl lead was the most active inhibitor with brain slices, and they were more sensitive to this salt than brei preparations were.

Triethyl lead did not combine with BAL or EDTA, and neither should be effective therefore in the treatment of tetraethyl lead poisoning.

*M. Patricia Fitzsimons*

OSHIMA, M. **[Studies on the Lead Poisoning. Part 2. On the Relation between Coproporphyrin in Urine and Lead Content of Urine and of Blood.]** *Shikoku Acta Med.* 1959, June, v. 14, No. 6, 25–34, 3 figs. [37 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"Variable laboratory diagnoses on lead poisoning were carried on 178 lead workers, and the relation between the coproporphyrin in urine and the lead content of urine and of blood was examined.

"1) It was impossible to find a close correlation between the coproporphyrin in urine and the lead content of urine and of blood, but the mean value of lead in urine and blood of all workers examined showed a certain degree of relationship to the coproporphyrin in urine.

"2) Many of workers engaged in their work for less than one year showed intense positive reaction to the coproporphyrin in urine. This finding suggests an excellent symptom to help detect at an earlier period a worker who has absorbed lead or a patient with latent lead poisoning.

"3) 12 workers out of 158 showed the specific gravity of whole blood under 1.049, and 10 out of 114 showed the hemoglobin value under 12.9 gr. per dl. Each of them amounted to about 8 per cent of all workers examined.

"4) 121 workers out of 178 (67·97%) showed positive reaction to the coproporphyrin in urine, and intense positive reaction signified by a figure (++) was observed in 43 workers (24·16%).

"5) Only 4 workers out of 146 (2.73%) showed more than 11 number of basophilic stippling per ten thousand of red blood cell. They also showed positive reaction to the coproporphyrin urine and that of three of them was intense."

MORRIS, G. E. Basisches Chrom-sulfat. Ergebnisse der Epicutantestung eines Chrom-III-Sa'zes. **[Basic Chromium Sulphate. Results of the Patch Testing of a Chromium III Salt]** *Berufsdermatosen.* Aulendorf. 1959, June, v. 7, No. 3, 126–31. [14 refs.]

In the diagnosis of the cause of "shoe-leather dermatitis" in which suspicion falls usually on the chromium compounds used in tanning, the substances commonly employed in patch testing of sensitivity are bichromates, chromium acetate or chloride or other chromium salts. The chromium compounds which are mentioned here do not, however, occur in leather.

The substance which is used for tanning of leather in the United States is the hydroxypentahydrate chromium sulphate—$[Cr(H_2O)_5OH]\ SO_4$. Its preparation is described, and it is recommended, on the evidence of some case reports, that it should be used in 0·2% solution in the patch testing of patients suspected of having "shoe-leather dermatitis". Another substance which may be used in testing is a lactosulphate of chromium which in some instances may be formed by the action of human perspiration on chromium compounds in leather.

Both the chromium compounds recommended for patch testing are trivalent and it is coming to be recognized that certain trivalent as well as hexavalent chromium compounds may be sensitizers [this *Bulletin*, 1959, v. 34, 355]. *M. E. Delafield*

SUZUKI, Y, NISHIYAMA, K., MATSUKA, Y., DOI, M., HIROSE, H. TAKANO, Y. & TAJIRI, T. **[Investigation on the Chronic Manganese Poisoning in the Manganese Mine. Report 5. Investigation on the Workers in the Manganese Mines (3).]** *Shikoku Acta Med.* 1959, July, v. 15, No. 1, 6–10. [17 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"In November 1956, an investigation was made on the workers at K. manganese mine. Previously, in 1950 and 1951, this mine had been examined by the present authors' department.

"1. For the workers inhalation of Mn dust seemed to be more dangerous than peroral ingestion.

"2. From the subjective and objective symptoms, it was confirmed that the symptoms which had been reported by us developed. Among them tremor of extremities and trunk, micrographia, and hyperhideosis were characteristic. They were observed in 30% of all workers.

"3. Erythropenia was observed in the workers with rather long careers (over 2–3 years). Many of the workers presented leucopenia. The percentage of neutrophile leucocytes, especially with segmented nuclei, was decreased and those of eosinophile and lymph cells were increased characteristically.

"4. The workers who presented indisposition relatively early after employment left their position at a much higher rate as compared with others.

"5. Description was also made of one case which was diagnosed as Mn poisoning."

HARRIS, W. B. & KINGSLEY, I. **The Industrial Hygiene of Uranium Fabrication.** *Arch. Indust. Health.* Chicago. 1959, May, v. 19, No. 5, 540–65, 8 figs.

In the handling of uranium the hazard to health is the inhalation of fine particles. Hence injury may arise from those operations where the material is finely divided or where oxidation has taken place and the oxides are raised into the air. Uranium reacts rapidly and easily with oxygen, so that substantially all processes in which heat is generated can result in such dispersion.

The authors have studied various operations in the processing of uranium. These include rolling, forging by means of either a hammer or a press, extrusion, drawing, machining and powder pressing. In some instances the experience was gained in production plants on full time operations, while in others the work was done on production-sized units but in experimental lots.

In this paper the experiences so gained are summarized. The effectiveness of various procedures for controlling occupational exposures is evaluated, and recommendations are made which are based on the results obtained during various conditions of operation.

Also included are specific recommendations for general procedures such as the disposal of waste, air cleaning, housekeeping, and personal hygiene. *Thomas Bedford*

LIPPMANN, M. **Environmental Exposure to Uranium Compounds. Air, Urine, and Medical Findings.** *Arch. Indust. Health.* Chicago. 1959, Sept., v. 20, No. 3, 211–26, 11 figs. [13 refs.]

If urine sampling is to be a test of safety in the processing of uranium it should be possible from a sample to recognize uranium exposure or body burden. This analysis, based on 3,000 air samples and 1,000 pairs of urine samples taken in a refinery in 1950–51, showed no useful correlation between air concentrations of soluble compounds and urine samples taken at the end of the working week, or between concentrations of insoluble compounds and samples taken after the 48-hour weekend. Moreover, the latter samples, usually thought to estimate long-term excretion of stored uranium, with a safety standard of 67 $\mu$gm. per litre, overestimated this.

Monthly average air dust exposures to the soluble compounds, $UF_6$ and $UO_2F_2$, reached 3,500 $\mu$gm. per $m^3$. In 29 men so exposed, the median before-weekend sample had 900 $\mu$gm. per litre, the highest 13,200. 3 men had urinary abnormalities but none had renal hypofunction.

From 8 men handling the insoluble compounds, $UO_2$ and $UF_4$, in concentrations reaching 9,700 $\mu$gm. per $m^3$, reduced by 75% by means of respirators, 8 of 33 after-weekend samples contained over 67 $\mu$gm. per litre, the highest 108; from men working in concentrations reaching 4,400, only 1 sample in 118 exceeded the standard.

After heavy exposure uranium excretion decreased for several weeks steadily, and concentrations should be predictable if the first-day excretion rate is known. This was confirmed from data of the men who had worked on the 2 plants for some time, before-weekend concentrations being equivalent to first-day, and after-weekend concentrations to third-day excretion. A comparison made of before-weekend concentrations and the differences between these and after-weekend concentrations showed a constant relation whether from exposures to soluble or insoluble compounds. An exposure to soluble uranium in the preceding weeks would augment the after-weekend's supposedly long-term excretion. This and other variables suggest that only samples taken after a vacation would indicate steady-state excretion reliably.

*M. Patricia Fitzsimons*

PETERSON, J. E. **An Approach to a Rational Method of Recommending Face Velocities for Laboratory Hoods.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No 4, 259–66, 4 figs. [21 refs.]

An equation for calculating face velocities which could be recommended as specific for each laboratory hood has been tested by experience and found to be valuable. Specifications for the "standard hood" and techniques for assigning numerical values to the factors are discussed and translated into mathematical formulae.

The function of exhaust hoods is to prevent contaminated air reaching the person working at the hood face. The main route by which air escapes is through the hood face. The efficiency of a hood depends on the behaviour of air at the face opening. The usual criterion is the mean face velocity, often specified as a single figure, but important variables are involved, mainly the toxicity and volatility of the materials to be handled, the effects of air disturbance outside and inside the hood, the characteristics of the hood itself and the variability of air flow at the face. Ranges of face velocities found in the literature could be divided into 2, those for materials of low toxicity beginning at 50 lineal feet per minute (f.p.m.) and those of high toxicity beginning near 100 f.p.m.

Velocities falling between these extremes were modified by 3 factors combining some variables: a vapour control factor, directly proportional to the vapour pressure multiplied by the molecular weight and inversely proportional to the control concentration; an environment factor proportional to the expected air disturbance; and a hood characteristic factor proportional to the size and shape of the opening. Variability of air flow at the face can be calculated from the measurements which are generally available for determining mean face velocities; but a table of variances is reproduced for hoods of different types. *M. Patricia Fitzsimons*

WILLIAMS, J. W. **The Toxicity of Trichloroethylene.** *J. Occupational Med.* Chicago. 1959, Oct., v. 1, No. 10, 549–54. [48 refs.]

COHEN, A. E., SCHEEL, L. D., KOPP, J. F., STOCKELL, F. R., KEENAN, R. G., MOUNTAIN, J. T. & PAULUS, H. J. **Biochemical Mechanisms in Chronic Carbon Disulfide Poisoning.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug, v. 20, No. 4, 303–23, 13 figs. [51 refs.]

This is a full account of a prolonged comprehensive experiment to determine the relationship between inhalation of $CS_2$ and the pathological lesions which develop. Rabbits were exposed for 6 hours a day on 5 days a week to 250 p.p.m. $CS_2$ in the anticipation that in about 3 months hind leg paralysis would occur. However, the concentration in the 17th week was increased to 500 p.p.m. and in the 22nd to 750 p.p.m. and this was maintained for another 17 weeks before all the rabbits had developed clinical signs of toxicity.

The early metabolic disturbances were reflected in failure to gain weight during the first 11 weeks, but the animals then compensated for the stress and gained. The earliest toxic sign was progressive loss of weight beginning in the 24th week, followed 6–14 weeks later by loss of muscular control over voluntary movements of the lower part of the back and hind legs. As this occurred animals were removed from exposure. Some were killed immediately; others were observed for 4–6 weeks, and gained weight, before being killed. Little or no recovery of function was observed, though there was improvement in tissue zinc and copper levels. Lesions were present in the cerebral meninges, the cortex, cerebellum and spinal cord, particularly in the upper thoracic portions occupied by the pyramidal tracts. The sudden loss of weight which preceded obvious toxic signs may be of prognostic value.

From the evidence of the numerous investigations the authors outlined the biochemical mechanisms. The $CS_2$ in the blood slowly reacts with amino groups of amino acids and protein to form thiocarbamate which cyclizes to thiazolidone; these newly formed complexing groups chelate polyvalent inorganic ions so that cellular metabolism is disturbed and the use of amino acids prevented; the interference with metabolism causes an adrenal stress response and a shift in metabolism which results in loss of weight and mobilization of fat stores; the cells most vulnerable fail in function and die, producing signs of injury. *M. Patricia Fitzsimons*

ŠVESTKOVÁ, V., ŠVESTKA, B. & FRAJBIS, Z. Hygienische Bewertung der Gefährdung der Arbeiter einer Generatoren-Station durch chronische Einwirkung von Kohlenoxyd. [**Long Continued Exposure to Carbon Monoxides—its effect on the Health of Workers at a Gas Generator Station**] *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 339–55, 1 fig. & 6 diagrams.

The problem of acute carbon monoxide poisoning in industry has to a large extent fallen into the background and attention now tends to be focused on the effects on health of years of exposure during work to an atmosphere which always contains a sub-toxic and occasionally a toxic concentration of the poisonous gas.

The investigation described in this paper was carried out in a large generator station where producer gas containing 25–30% of carbon monoxide, and also other gases which may be harmful, is made for use in the associated steel works. Some technical details of the method used to generate the gas from coal are given together with some account of the general conditions under which the employees work.

227 samples of air taken from the workplace during different months of the year were analysed to determine the carbon monoxide concentration. This concentration which was found to range from 0·004 to 1,700 mgm. per litre of air, fell below the maximum permissible limit of 0·036 mgm. per litre in only about 19% of samples in May and 48% in October. Blood samples taken from some of the workers after some hours of their shift showed in every case an increase of carboxyhaemoglobin which exceeded normal limits in over 50% of the men.

The medical records of the 46 men engaged in the work were scrutinized. Their average age was 45·2 years and they had been at generator work for an average period of 14·4 years ranging from 2 to 38 years. Acute severe carbon monoxide poisoning had occurred in 16 men who had later been able to return to work. There is a considerable description of the medical findings at the routine examinations which were begun some years ago but in no worker was the clinical picture of chronic carbon monoxide poisoning as reported in the literature found to be present. *M. E. Delafield*

RIPPERTON, L. A. & JOHNSTON, D. R. **Effects on Growing Animals of a Continuous Exposure to Experienced Concentrations of Nitrogen Dioxide.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No. 4, 324–6.

This study was planned to investigate the effects of long term exposure to $NO_2$ in quantities present in a polluted urban atmosphere. Rats were exposed continuously, except for servicing and urine collection, to $NO_2$ in concentrations of 0·5 p.p.m. and less for periods up to 6 weeks.

There was no difference in the microscopic appearances of the tissues examined, lung and liver, from exposed or control animals. Both groups showed signs of endemic virus pneumonia. Blood catalase values differed as the experiment went on. Urinary excretion of glutamic acid and of aspartic acid were higher in the experimental group. An incidental observation was that at 6 weeks the serum of 2 rats appeared milky. Another was that there was delay in littering during the pilot study.

During the experiment sporadic insecticidal spraying was discovered, and this as well as the pneumonia made interpretation of the data speculative. The results, some significant and some surprising, suggest that the differences between the control and experimental animals may be attributed to the $NO_2$, but they may not occur with healthy animals. Carcasses and serum are being analysed and further investigations are proceeding.

*M. Patricia Fitzsimons*

GIUGGIOLI, A. Indagini sperimentali sulle intossicazioni da bromo: alterazioni dell'-apparato respiratorio e orientamenti terapeutici con iposolfito di sodio. [**Experimental Bromide Poisoning; Respiratory Changes and Treatment with Sodium Hyposulphite**] *Rass Med. Indust.* Rome. 1959, Mar.–Apr., v. 28, No. 2, 103–51, 14 figs. [Numerous refs.] English summary (9 lines).

This is a very long paper in which, after an extensive introductory portion on the properties and effect of bromine on human beings, a detailed report is given of experiments on rabbits and guineapigs. These animals, in closed boxes of 1 cubic metre size, were made to inhale varying concentrations of bromine for varying lengths of time so as to simulate both acute and chronic poisoning. They were then killed and the organs, especially the respiratory apparatus, carefully examined. Some were treated after the exposure by the inhalation of a saturated solution of sodium hyposulphite.

Rabbits proved to be more sensitive than guineapigs, though on post-mortem all the animals showed the effects of the halogen on the respiratory tract to a marked degree. In those guineapigs treated with sodium hyposulphite 8 of 12 recovered and after about 10–15 days had quite returned to normal, although they had shown symptoms of poisoning as grave as those in the untreated guineapigs.

The author concludes that the favourable results obtained by the hyposulphite treatment warrant further experiments. *W. K. Dunscombe*

WILDING, J. L., SMITH, W. J., II, YEVICH, P., SICKS, Mary E., RYAN, Stella G. & PUNTE, C. L. **The Toxicity of Boron Oxide.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No. 4, 284–9, 3 figs. [15 refs.].

One of the main solids in the exhaust from jet engines is boron oxide ($B_2O_3$), though being an anhydride it reacts exothermically with water to form boric acid.

Numerous and varied chemical analyses and histological examinations carried out in rats at intervals of 2 weeks, and serial blood counts, blood analyses and liver function tests in dogs are described, together with local effects in rabbits.

Rats were exposed to aerosols of $B_2O_3$ in dynamic exposure chambers for 24, 12 and 10 weeks and dogs for 23 weeks for 6 hours daily on 5 days a week. The respective concentrations were 77, 175, 470 or 57 mgm. per $m^3$. There were no deaths or toxic signs from inhalation. Some rats exposed to 470 mgm. per $m^3$. had a red nasal exudate, probably from scratching because of the dust. No changes from control values were found in the investigations, which included bone fragility tests and X-ray examinations, except in rat urine: increased volume, creatinine excretion and boron content and a lower *p*H. There was a slight, probably insignificant, leucocytosis in the dogs.

Rats refused to drink water containing 1 or 1·5% by weight of $B_2O_3$ and lost as much weight, 40%, as controls deprived of water, for 10 days; this was regained rapidly and steadily when tap water was given. 2 groups given water containing 0·5 or 0·25% lost weight, but the second group slowly regained it. Intragastric intubation of a 10% mixture on 5 days each week for 3 weeks had no noticeable effect.

In rabbits the application of 1 gm. of $B_2O_3$ dust to 25 $cm^2$. of the clipped, wet skin caused erythema which persisted for 2–3 days, and 50 mgm. applied to the eye caused almost immediate conjunctivitis.

*M. Patricia Fitzsimons*

TALWALKAR, C. V. **Dye Poisoning in Dock Workers.** *J. Ass. Physicians India.* 1959, Sept., v. 7, No. 5, 363–73, 4 figs. [25 refs.]

This investigation of cargoes showed that 34 patients admitted to hospital in Bombay at intervals became ill after handling unsafely packed or unsafely stowed consignments of dyes. The men worked with bare hands and feet, unloading ships or loading lorries. Most of them had unloaded only steel plates yet they absorbed 5-chloro-*ortho*-toluidine incidentally. This caused haematuria, pain, giddiness, headache, vomiting, dysuria or, unexpectedly, polyuria. Drums of paint unloaded from an earlier ship by the first patients contained this compound. Lorry loaders who absorbed *m*-dinitrobenzene when they repacked spilt crystals from damaged casks, and men who unloaded drums of aniline oil from a third ship, became cyanosed and unconscious, and the loaders also had neck rigidity. Cleaners in the third ship had giddiness. All recovered.

In the second ship, steel plates coated with anti-corrosive jelly were stowed in several hatches. Drums of liquid containing the toluidine compound and casks of *m*-dinitrobenzene crystals were stowed at Genoa between decks and also on top of plates in the badly ventilated deep tank of number 4 hatch next to the engine room. Directions on the drums advised stowing away from boilers. Screw-type bungs about half way down the sides of the drums were leaking and a damaged drum was almost empty. A member of the crew developed fatal haemorrhagic cystitis after entering the deep tank at Karachi. Plates removed from hatch 4 had discoloured coatings which contained aromatic amido compounds.

It is recommended that drums, filled to 80% capacity, should have top bungs and that aniline dyes should be stowed away from heat, food and crews' quarters. Skin absorption should be prevented by protective clothing and washing facilities. Where necessary respirators should be provided. A high fluid intake is necessary. [Some references are not clear].

*M. Patricia Fitzsimons*

CARPENTER, H. M.; JENDEN, D. J.; SHULMAN, N. R.; TUREMAN, J. R.; FRIESS, S. L.; BALDRIDGE, H. D.; KNIGHT, C. E.; PREZIOSI, T. J. **Toxicology of a Triaryl Phosphate Oil. I. Experimental Toxicology** [CARPENTER, JENDEN, SHULMAN & TUREMAN]. *Arch. Indust. Health.* Chicago. 1959, Sept., v. 20, No. 3, 234–52, 10 figs. [36 refs.] **II. A Quantitative Study of Toxicity in Different Production Batches** [FRIESS, JENDEN & TUREMAN]. *Ibid.*, 253–7, 2 figs. **III. Human Exposure in Operational Use Aboard Ship** [BALDRIDGE, JENDEN, KNIGHT, PREZIOSI & TUREMAN]. *Ibid.*, 258–61, 1 fig.

I. The lubricating oily liquid (TCP-1), a tricresyl phosphate preparation (TCP), investigated for use in hydraulic systems in aircraft carriers, is a mixture of phosphate esters of cresols, xylenols and other alkyl phenols. A summary is given in the first study of the properties of the batch tested by repeated administration to chickens orally; to rabbits orally, subcutaneously, percutaneously and by inhalation; and to dogs subcutaneously. TCP-1 was made from cresylic acid which contained less than 1·5% of orthocresol.

II. In the second study 6 batches were compared with triorthocresyl phosphate (TOCP) by means of a points system developed in the first paper for serial quantitative testing in chickens of the qualitatively similar paralytic activity of the 2 compounds. This method showed TCP-1 to have an activity equivalent to 21% TOCP, which indicated that TCP-1 contained additional substances which caused paralysis or potentiated TOCP paralysis. Statistical variation in results was mainly due to 1 batch which had an activity equivalent to more than 25% TOCP. Its cresylic acid source was coal tar, not, as with other batches, mainly petroleum. The infra-red spectra of different batches were alike, and all differed from the TOCP spectrum. An improved chicken assay by means of one 15th-day group test is suggested.

Paralysis in all species was greatest in chickens. Blood cholinesterase levels were depressed in rabbits and dogs, and results attributable to this were most marked in rabbits. Dogs developed abscesses at the injection sites and acute congestive heart failure. No local effects occurred in skin or respiratory tract. Systematic effects by all routes were similar in kind, ingestion in rabbits being the most dangerous. No pathological changes were seen in central or peripheral nerve tissues. Testicular atrophy, muscle degeneration and bronchopneumonia suggested interference with vitamin E metabolism.

III. The ship-crew survey during 3 months' operational use, with concentrations of 0·1 p.p.m. TCP-1, revealed no abnormalities in clinical examinations, blood

counts or cholinesterase estimations. Skin irritation attributed to heat was not aggravated by TCP-1, even though 5 subjects had skin sensitivity to other agents. Other men contaminated while clearing spilt TCP-1, without this being known for 24 hours, did not remove saturated dungarees. Their cholinesterase values were not significantly below the survey subjects' mean levels. A smaller shipyard survey was also negative.

*M. Patricia Fitzsimons*

HENSON, E. V. **The Toxicology of Some Aliphatic Aldehydes.** *J. Occupational Med.* Chicago. 1959, Aug., v. 1, No. 8, 457–62. [26 refs.]

Some general pointers only are taken from the many details of action, chemistry, experiments and uses given in this 3rd review of the series on aliphatic hydrocarbons. Aldehydes, intermediate products in the oxidation of alcohols to acids, are irritating and toxic but the local irritation probably prevents dangerous exposures, particularly with the more toxic unsaturated compounds acrolein and crotonaldehyde which are lachrymators.

In saturated aldehydes, $C_nH_{2n}O$, the carbonyl group C=O has a hydrogen and alkyl radicle attached, and some of the unusual features of formaldehyde are perhaps due to its having 2 hydrogens. The word aldehyde is said to be a contraction of the words alcohol dehydrogenated, and unless modified by a prefix signifies acetaldehyde. This and glycoaldehyde are normal metabolic products. It is thought that blocking agents for treatment of alcoholism hold up the metabolism of alcohol at the aldehyde stage and that the accumulation of acetaldehyde causes the associated unpleasant symptoms. Chronic intoxication by the aldehydes, judging by the absence of reports, seems not to occur. This is interesting in view of their ubiquity in every day life, exhaust fumes on the roads, onions and burning fat in the home, etc. Formalin is a solution of formaldehyde in water and methanol. In water aldehydes probably exist in equilibrium with their hydrates, an exception being stable, crystalline chloral hydrate. Being reactive, lower aldehydes form polymers: paraform, paraldehyde and metaldehyde are examples in general use. Aldehydes, especially formaldehyde, can produce cutaneous and systemic allergic reactions, but aromatic aldehydes and conjugated aliphatic aldehydes seem not to do so.

Aldehydes vary from gaseous formaldehyde to solids at $C_{12}$. Toxicity, irritant and anaesthetic action, solubility in water and sharpness of odour decrease with length of carbon chain.

Because of their industrial importance, formaldehyde, acetaldehyde, paraldehyde, acrolein, crotonaldehyde and glyoxal, a dialdehyde, are discussed in detail.

*M. Patricia Fitzsimons*

WILSON, R. H. & WILSON, G. L. **Toxicology of Diisocyanates.** *J. Occupational Med.* Chicago. 1959, Aug., v. 1, No. 8, 448–50.

These irritants are used in the manufacture of versatile polymers known as polyurethanes for such products as adhesives, rigid and elastic foams, plastics and synthetic rubbers [see this *Bulletin*, 1959, v. 34, 1141]. Among the group used in industry are toluene diisocyanate, either the 2,4 or the 2,6 isomer or a mixture (TDI), *p*-phenylene diisocyanate, methylene bis (4-phenyl isocyanate) and 1,5-naphthalene diisocyanate. This article includes precautions, based on experimental studies and industrial use of TDI.

The threshold limit for TDI of 0·1 p.p.m. calls for well designed equipment and good local exhaust, especially as the least detectable odour was at 0·4 p.p.m. while nose and throat irritation was noticed at 0·5 p.p.m. Though in animals the acute toxicity is not high, TDI is a powerful irritant to eyes, skin, gastrointestinal tract and respiratory tract, with the possibility of cumulative effects. Acute inhalation studies in several species revealed pulmonary congestion and oedema, and subacute exposure resulted in tracheo-bronchitis. In man, in addition, asthma-like symptoms indicate inhalation sensitization. Hardening and darkening of the skin has been observed.

Accidental contact with water, acids and alkalis must be prevented. $CO_2$ may be evolved. If, notwithstanding good handling and engineering practices, spills occur, a decontaminant is an aqueous 5% ammonia solution containing 10% isopropyl alcohol. Floor draining and hoses should be provided.

Eyes if contaminated should be immediately irrigated with water for 15 minutes and the patient should be referred for medical treatment. Contaminated clothing should be removed and the skin washed first with 30% isopropyl alcohol, then with soap and water, possibly by shower-bath.

Medical selection and supervision should include the use of pre-placement and periodic X-ray examinations of the chest. Abnormal lung findings or a history of allergy are a bar to potential exposure, and the development of respiratory symptoms or of peribronchial infiltration necessitates removal from the work, in most cases permanently.

*M. Patricia Fitzsimons*

NAGASUE, D. [**Study on Prophylactics for Parathion Poisoning. Part 1. Influence of 1-Butyl-3-p-Tolyl Sulfonyl Urea (D860) on Experimentally Poisoned Dogs**] *Igaku Kenkyu.* Fukuoka. 1959, Sept., v. 29, No. 9 (Extra Edition), 3191–209. [23 refs.] [**Part 2. Preventive Effect of Benzene Sulfonic Amide Derivatives on Experimentally Poisoned Mice**] *Ibid.*, 3210–23. [18 refs.] [In Japanese.]

The English summaries appended to the paper are as follows:—

i. "After examining the preventive effect of $D_{860}$ (1-butyl-3-p-tolyl sulfonyl urea) against parathion poisoning of adult dogs and influence on parathion poisoned dogs, the following results were obtained:

"1. Some healthy adult dogs were injected subcutaneously with parathion emulsion which was made at Nihon Tokushu Noyaku (Japan Special Agricultural Chemicals Mfg. Co.) and diluted by 50 times in water. Each of the dogs was given 4.0 cc/kg (37.3 mg/kg) of ethyl-parathion and within 11 hours all of them were found dead.

"2. When the dogs were poisoned, the values of cholinesterase activity fell, and the values of blood sugar and serum diastase rose. This phenomenon was

especially marked just before they were going to die. Some of the dogs survived even after they suffered from such toxicosis. In this case their cholinesterase activity values and other values returned to normalcy within 15 days at the latest.

"3. When 100 mg/kg of $D_{860}$ had been given the dogs through mouth 2–4 days before the subcutaneous administration of lethal dose (4.0 cc/kg) of aqueous dilution of parathion, three of the five dogs survived. And when 150 mg/kg of $D_{860}$ had been given the other group of dogs 12 hours before the administration of the same lethal dose, the same result was obtained. Here the administration of 150 mg/kg of $D_{860}$ 12 hours before was found to be far more effective than that of 200 mg/kg 3 hours before. It was considered that, when the density of $D_{860}$ in the blood reaches its climax in three hours after its oral administration, $D_{860}$ undergoes some kind of change and acts as neutralizer, or by influencing some other thing, it exhibits its effect through this other thing.

"4. It appeared that the preventive effect of $D_{860}$ against parathion poisoning had almost nothing to do with its influence on the cholinesterase activity, blood sugar and serum diastase.

"5. When $D_{860}$ was given through mouth, more dogs survived than when it was not. At the same time their clinical symptoms were found milder, and some of the characteristic symptoms failed to appear. Above all, the disappearance of spasm was noteworthy."

ii. "The lethal quantity of parathion to a male mouse of DD stock was decided; then that of benzene sulfonic amide and p-carboxy benzene sulfonamide. Out of these three derivatives 14 kinds of drugs were prepared, and their preventive effect against parathion poisoning together with that of 2-pyridine aldoxime methiodide was studied. The following was the result thus obtained.

"1. Parathion emulsion which was made at Nihon Tokushu Noyaku (Japan Special Agricultural Chemicals Mfg. Co.) and diluted by 600 times in water was subcutaneously administered to some healthy mice of DD stock. When 15 cc/kg (11.65 mg/kg) was given to 6 mice 5 of them died within 6 hours, and one survived for a long time. When 20 cc/kg (15.53 mg/kg) was given to the same number of mice all of them died within 90 minutes.

"2. Preventive effect against parathion poisoning was not found to exist in 1-butyl-3-p-aminobenzene sulfonyl urea, sulfanil amide, and 3-4-dimethyl-5-sulfanil amidoisoxazole which belong to the sulfonyl amide derivatives.

"3. Some of the p-methyl-benzene sulfonic amide derivatives had the preventive effect. Among them 1-butyl-3-p-tolyl sulfonyl urea ($D_{860}$) ranked first in its intensity of effect, followed by p-toluene sulfon amide. N-acetyl-p-toluene sulfon amide and 5-methyl-3-p-tolyl sulfonyl amidoisoxazole were found to be as powerful as or a bit less powerful than p-toluene sulfon amide, because a comparatively large amount of 400 mg/kg of these two was required to make them effective. Almost no preventive effect was noticed in p-toluene sulfonic acid, and totally no effect in sulfonyl amidoisoxazole and 5-phenyl-3-p-tolyl sulfonyl amidoisoxazole.

"4. Among the p-carboxybenzene sulfon amide derivatives, 1-butyl-3-p-carboxyphenyl sulfonyl urea had a slight preventive effect, but p-carboxybenzene sulfon amide has no effect at all.

"5. 2-pyridine aldoxime methiodide (PAM) had nearly as strong a preventive effect as $D_{860}$."

BRAUN, Werner. Chlorakne. Akneartige Hautveränderungen durch chlorierte aromatische Kohlenwasserstoffe. [**Acneiform Skin Changes due to Chlorinated Aromatic Hydrocarbons**] *Berufsdermatosen.* Monograph Vol. 1. 73 pp., 30 figs. on 15 pls. 1955. Aulendorf i Württ: Editio Cantor, Germany. [DM.12.80]

This is the first of a series of monographs on industrial skin diseases which are to appear in association with the journal *Berufsdermatosen* (Occupational Dermatoses).

In the introduction the author writes about the problem of industrial skin diseases in general which form so high a proportion of the total of the industrial diseases at the present day. The subject of the skin disorders, which may result from exposure of workers to chlorinated hydrocarbons in a number of industrial processes, is considered by review of the literature of the period 1899–1954. These skin conditions have come to be called chloracne although a variety of different names have been assigned to them in accordance with the particular chemical which has been the cause. As the skin disorder is not a simple acne a designation to cover all cases might be "acneiform skin changes due to chlorinated aromatic hydrocarbons". Sections of the monograph contain lists of the chemicals which cause chloracne and descriptions of its clinical features, treatment, prevention and histological appearance of the skin.

In the second part of the monograph there is an account of the results of published experimental work on man and animals. The author's experimental work is also described with some very good photographs of the macroscopic and microscopic appearances of chloracne.

This monograph with its list of 138 references is an excellent publication. *M. E. Delafield*

SCHULTHEISS, Eberhard. Gummi und Ekzem. [**Rubber and Eczema**] *Berufsdermatosen.* Monograph Vol. 3, 213 pp., illustrated. 1959. Aulendorf i Württ: Editio Cantor, Germany. [DM.19.80.]

This book is Monograph 3 in the series of the journal *Berufsdermatosen* (Occupational Dermatoses). Its author has had great experience of skin diseases among workers in rubber in Hanover which is the main centre of the rubber industry in West Germany.

This publication is a compendium of detailed information on rubber and the medical risks to which workers in the industry are exposed. There is a review of the medical literature on these risks which include the so-called "rubber eczema" from direct exposure to chemical substances used in the industry or by contact with finished rubber articles, leucodermia, chloracne, zinc oxide acne, alopecia, urticaria and allergic

asthma. This review is followed by an account of the conditions under which eczema may arise, some case histories, and details of diagnosis. Skin tests are described with very long lists of the substances which should be applied. A section of the monograph deals with the chemistry and technology of natural and synthetic rubber in which a large number of chemicals are used as vulcanizers, accelerators, plasticisers and so on.

A number of indexes are given on: (1) the chemicals used in the rubber industry in 79 pages, (2) medical terms and chemicals in 10 pages and (3) references to the literature, 213 in number.

This is an excellent monograph. *M. E. Delafield*

SCHULTHEISS, E. Überempfindlichkeit gegenüber Hydrazin. [**Hypersensitiveness to Hydrazine**] *Berufsdermatosen.* Aulendorf. 1959. June, v. 7, No. 3, 131–6. [10 refs.]

In this paper a case of hypersensitivity to hydrazine in a 61-year-old male employee at a power station is described. He suffered a severe eczematous condition of the hands and arms from contact with hydrazine and was also sensitive to a substance (tetramethylthiuramdisulphide) used in the manufacture of the rubber gloves which were worn at work. Patch testing showed that in addition to being sensitive to hydrazine hydrate in a dilution of 0·015% the patient reacted also to isonicotinic acid hydrazide [isoniazid], potassium dichromate, trivalent chromium chloride and nickel sulphate.

There is an account of the preparation and properties of hydrazine and of its many uses in industrial processes. The case is discussed from its chemical aspects. *M. E. Delafield*

THOMA, G. E., Jr. & WALD, N. **The Diagnosis and Management of Accidental Radiation Injury.** *J. Occupational Med.* Chicago. 1959, Aug., v. 1, No. 8, 421–47, 4 figs. [30 refs.]

A long and generally useful article: it gathers together facts and makes recommendations for diagnostic procedures and management in the rare but increasingly frequent acute radiation syndrome. An account is given of the 30 persons affected by the 7 reactor major criticality accidents since 1945 in America, Russia and Yugoslavia. Accidents of this type arise when the level of intensity of a nuclear reaction exceeds a critical level, and they produce variable intensities of fast neutrons and gamma rays. The radiation exposures were acute, external, penetrating and generalized. The first collision dose to each patient is defined and is specified in rad.

An analysis of the circumstances and dosimetry of each accident and an analysis of the clinical signs, symptoms and course, laboratory findings and treatment of each patient are supplemented by 5 hypothetical illustrative case reports. Each report describes most of the possible characteristic phenomena which could be found day by day in one of the 5 radiation injury groups into which the patients were divided according to the degree and course of symptoms and signs of the illness. This grouping was designed to clarify an approach to individual patient management because of the difficulty, in accidents of this complexity, in obtaining quick and accurate dose estimates and because of the variation in individual response to similar doses, even though the broad relationship recognized between magnitude of exposure and severity of clinical sequelae is also described.

Investigations which would facilitate research in diagnostic measures are listed and the diagnostic use of a profile scoring method is given in some detail.

An attempt was made to identify those findings which in these cases had the greatest early prognostic value. It is suggested that by taking note of the time of onset and duration of symptoms and by assessing daily full blood counts it should be possible within 72 hours to recognize those patients who should still be kept in hospital for supportive and symptomatic treatment. [See also this *Bulletin*, 1959, v. 34, 301.] *M. Patricia Fitzsimons*

# Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

## FOODSTUFFS

*Composition and Bacteriological Control*

PUBLIC HEALTH LAB. SERVICE. **The Examination of English Egg Products. A Report of the Public Health Laboratory Service.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Sept., v. 18, 158–61.

"In a study of samples of liquid and frozen egg from 25 packing stations (plus one at which samples were examined for salmonellae only) at intervals over a year, it was found that the colony counts varied widely from station to station. Counts varied also with the season of the year. Faecal coli were isolated from 74 per cent. of samples, and salmonellae from 1·2 per cent. of samples. In an unpublished study of large-scale English frozen egg plants made at the same time it was found that 2·6 per cent. of 786 samples yielded

salmonellae, and in a study of imported frozen egg in 1955–56 (Report 1958) 7 per cent. of samples yielded salmonellae. Egg products from small producers appear therefore to be less likely than products from large producers to be contaminated with salmonellae."

NILSSON, Gerda. **Reducing Properties of Normal and Abnormal Milk and their Importance in Bacteriological Grading of Milk.** *Bact. Reviews.* 1959, June, v. 23, No. 2, 41–7. [19 refs.]

The methylene blue and allied reduction tests are very extensively used to assess the keeping quality and other factors of milk, and as such these tests are very valuable. All workers must, however, have recognized that they are rather of a "hit and miss" character, as so many factors are involved which are associated with quite different components in the milk. The author of this valuable paper particularly recognizes this problem and the article is mainly concerned with these different factors. "Milk constitutes a complicated biological system embracing many redox systems of different concentrations and compositions", while, in addition, infected milk contains the redox systems of the micro-organisms concerned. This, to a considerable extent, is a new and most useful approach and the paper is concerned with a detailed consideration of these different factors in both normal milk and milk from cows infected with mastitis. It is impossible to give a detailed summary of the article as many important findings are merely set out as results from various quoted papers (many by the author) and the actual experimental findings are not given. There is no doubt of the value of the work done and the papers (and if possible the references) should be read in their entirety. Work along these lines may result in a clearer understanding of the various factors involved and in the end give these tests a real scientific basis.

Some examples will make this clearer. For instance, the author states that in normal milk at least 4 reducing systems are known. Considerable space is devoted to the role of enzymes, hydrogen donators and precursors in redox properties of normal and mastitis milk. For mastitis milk, the influence of a number of new factors must be estimated. For instance, it was possible to demonstrate the existence of a higher concentration of the enzyme xanthine oxidase in mastitis milk than in normal milk. The reducing properties of mastitis-causing organisms—many varieties of streptococci, staphylococci and coliform organisms—exert some influence. The experiments quoted suggest that this may be greater than is usually accepted, particularly with coliform organisms.

The author goes rather further in suggesting the possibility of detecting the effect of mastitis infection on milk by means of biological tests such as the xanthine oxidase test and the Schardinger test. Such a possibility is, however, rather for the future, and indeed Nilsson agrees that this will depend on a number of factors, which are set out.

It will be appreciated that the scope of the discussions included is to a considerable extent, along new lines and as such is of high value. *W. G. Savage*

ORTENZI, R. & MONDINO, G. Contributo alla ricerca del micobatterio della tubercolosi nel latte pasteurizzato. [*Myco. tuberculosis* **in pasteurized milk.**] *Nuovi Ann. d'Igiene e Microbiol.* 1959, May–June, v. 10, No. 3, 201–8. [28 refs.] English summary (8 lines).

Milk pasteurized at 2 large plants (indicated as A and B) in Perugia was tested as follows: 5 half-litre bottles were examined daily for 20 days from each plant, the samples being taken in January, February, March and October 1957. 100 cc. was taken from each bottle, centrifuged for 30 minutes at 4,500–5,000 r.p.m., the cream and the deposit taken up in 3 cc. saline, heated for 2–3 minutes at 40–42°C. in a water bath, and then equal amounts were inoculated subcutaneously into 3 guineapigs. The animals were kept under observation for 3 months when the survivors were killed, autopsied, and examined for acid-fast organisms and cultures taken. If positive these were again tested biologically on rabbits and hens and 5 other guineapigs.

Acid-fast organisms were found in 20 samples from A and 2 from B; all caused abscesses at the point of inoculation in guineapigs and 2 both inguinal and lumbar adenitis. The organisms grew on Petragnani's medium in 48 hours and all were resistant to PAS 1,000 μgm./cc. and isoniazid 100 μgm./cc.

The authors state that no *Myco. tuberculosis* was isolated and the acid-fast organisms detected were only saprophytic mycobacteria.

[The method of pasteurization is not given.]

*W. K. Dunscombe*

FREEDMAN, M. L. & MEARA, P. J. **Antibiotic Contamination of Milk Supplies as a Veterinary and Public Health Problem.** Reprinted from *South African Practitioner.* 1959, v. 5, Nos. 1, 2, 3 & 4, 16 pp. [Numerous refs.]

This is a clear and detailed review, with many references, of the veterinary and public health problems which may arise from milk supplies contaminated with antibiotics which are widely used in the intramammary treatment of cows suffering from mastitis. These problems lie particularly in (1) the manufacture of cheese and cultured milk products in which the normal growth of starter cultures may be inhibited and (2) the harmful effects from which persons consuming contaminated milk may suffer through sensitization to penicillin and allergic manifestations.

A section of this review deals with: (1) the extent of antibiotic contamination of milk reported from different countries, (2) the degree of antibiotic contamination which is harmful to cheese manufacture, (3) the period of excretion of antibiotic after intramammary treatment, (4) the pasteurization of contaminated milk, a method which does not inactivate penicillin appreciably, (5) the testing of milk for antibiotic contamination, (6) the preservative effect of antibiotics in the milk supply and (7) antibiotic inhibitors in milk.

Mastitis in relation to antibiotic therapy is considered at some length with particulars of its incidence which is still high and causes serious loss to dairy farmers, the changing bacterial aetiology of the disease and the

reports by various workers of the development of antibiotic-resistant strains of bacteria.

The hazards to health presented by milk supplies contaminated with antibiotics are discussed at length with some case histories and a description of the adverse reactions to penicillin and other antibiotics which may occur. Reference is made to warnings issued by the World Health Organization against the indiscriminate use of penicillin; the fact that the production of penicillin has increased from 29 pounds in 1943 to a present annual figure of 750 tons, and the estimate that by 1957 about 1,000 fatal reactions to penicillin had occurred in the United States.

There is also a detailed account of the measures that should be taken to overcome the antibiotic milk problem. *M. E. Delafield*

BURTON, H., FRANKLIN, J. G., WILLIAMS, D. J., CHAPMAN, Helen R., HARRISON, A. Jean W. & CLEGG, L. F. L. **An Analysis of the Performance of an Ultra-High-Temperature Milk Sterilizing Plant. IV. Comparison of Experimental and Calculated Sporicidal Effects for a Strain of** *Bacillus stearothermophilus. J. Dairy Res.* 1959, Oct., v. 26, No. 3, 221–6, 3 figs.

## FOOD POISONING

BOKKENHEUSER, V. & RICHARDSON, N. J. **The Bacteriology of the Bantu Food-Handler: Enterobacteriaceae.** *South African Med. J.* 1959, Sept. 19, v. 33, No. 38, 784–6. [12 refs.]

In 1958, 2,778 specimens of excreta were examined from 1,565 Bantu food-handlers, prospective or employed in 19 Transvaal gold mines.

75% supplied one specimen each of both faeces and urine. 25% submitted single specimens of either faeces or urine. Cultures were made on SS- and McConkey plates and in selenite liquid medium. Salmonellae or shigellae were isolated from 75 (4·8%) of persons; all cultures except 1 were of faecal origin and urine was considered to be of little value. Salmonellae (25 serotypes) occurred more frequently than shigellae (5 serotypes); *Salm. typhi* was isolated once only. There was little seasonal variation.

It was impossible to say whether the positive food handlers were chronic or transient carriers.

This method of bacteriological control was considered to be inadequate for establishing freedom from *Salm. typhi*; also a single negative sample of faeces is regarded as unsatisfactory for indicating the absence of organisms of the salmonellae and shigellae groups.

*Betty C. Hobbs*

KALLINGS, L. O., LAURELL, Anna B. & ZETTERBERG, B. **An Outbreak due to** *Salmonella typhi murium* **in Veal with special reference to Phage and Fermentation Typing.** *Acta Path. et Microb. Scandinavica.* 1959, v. 45, No. 4, 347–56, 3 figs. [13 refs.]

Approximately 500 cases of gastro-enteritis due to *Salmonella typhimurium* occurred in Sweden in 1956 to 1957. Imported frozen veal used for the preparation of a processed meat popular at Christmas time was said to be the source of infection.

*Salm. typhimurium* isolated from the veal gave the same bacteriophage and fermentation reactions as the strains isolated from the patients; 2 types were predominant, both had been concerned in outbreaks in the exporting country but had not been observed hitherto in Sweden.

*Salm. bovis morbificans* was also found in veal and patients.

The usefulness of the combined phage and fermentation typing of *Salm. typhimurium*, proposed by KALLINGS and LAURELL [this *Bulletin*, 1957, v. 32, 1189] is emphasized.

An interchange of strains enabled a comparison to be made between the phage typing methods of Great Britain and Sweden. *Betty C. Hobbs*

MACKEL, D. C., PAYNE, F. J. & PIRKLE, C. I. **Outbreak of Gastroenteritis caused by** *S. typhimurium* **acquired from Turkeys.** *Pub. Health Rep.* Wash. 1959, Aug., v. 74, No. 8, 746–8, 1 chart.

300 inmates of a penal institution showed symptoms of severe nausea, vomiting, cramps, diarrhoea and pyrexia (99·6° to 104°F.) following meals of cold roast turkey sliced on the same chopping block used for preparing the uncooked birds. Reheated meat from the same carcasses did not cause illness.

*Salm. typhimurium* was isolated from more than 100 affected persons and also from raw frozen turkey necks.

There was a good response to treatment with oxytetracycline; the number of positive stools dropped to 30% after 14 days, but one person was still excreting after 4 months.

SS agar was used for direct plating and brilliant green tetrathionate broth subcultured on to brilliant green agar for enrichment.

The examination of chopping blocks and utensils gave negative results.

Other workers have observed fowl as the vehicle of salmonella infection [this *Bulletin*, 1942, v. 17, 424].

*Betty C. Hobbs*

See also p. 195, LAMANNA, **The Most Poisonous Poison. What do we know about the Toxin of Botulism? What are the Problems to be solved?**

# Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma; Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

*Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the* TROPICAL DISEASES BULLETIN.

BURNS, J. & HOLTMAN, D. F. **Tennecetin: a New Antifungal Antibiotic. General Characteristics.** *Antibiotics & Chemotherapy.* New York. 1959, July, v. 9, No. 7, 398–405, 4 figs. [11 refs.]

Tennecetin, so called because the new species forming it, *Streptomyces chattanoogensis*, was cultivated from a sample of Tennessee soil, is a tetraene, and thus distinguished from a known group of antifungal antibiotics which are polyenes. This paper describes the characters of the organism, production, extraction and assay procedures, and some chemical and physical properties of the antibiotic. It inhibits the growth of all fungi which have been tested, of which a large number are listed, some in concentrations as low as 0·5 μgm./ml., but has little or no action on bacteria. *L. P. Garrod*

BARR, F. S. **Tennecetin: a New Antifungal Antibiotic. Toxicological Studies.** *Antibiotics & Chemotherapy.* New York. 1959, July, v 9, No 7, 406–8.

Tennecetin was administered by several routes to rabbits, rats, cats, mice, dogs and guineapigs. The LD50 by the intravenous route was low (20 mgm./kgm. in rabbits), the animal dying rapidly with convulsions. LD50 by the intraperitoneal, intramuscular and subcutaneous routes were in that ascending order of magnitude and in that increasing order of time to death, which occurred with respiratory paralysis. These findings contra-indicate parenteral administration of this antibiotic, but oral administration had no observed ill effects, and it is hoped that treatment of fungal infections of the skin, vagina and gastro-intestinal tract may prove feasible. *L. P. Garrod*

KIRK, Jacque'lyn & AJELLO, L. **Use of Griseofulvin in the Therapy of Tinea Capitis in Children. Preliminary Observations.** *Arch. Dermat.* 1959, Sept., v. 80, No. 3, 259–67, 1 fig.

118 Negro and 2 white patients aged from 2 to 16 years, all suffering from tinea capitis, were treated with a wide range of dosage schedules of griseofulvin. The lowest dosage, calculated on a body weight basis, was 3·1 mgm. per lb. per day and the highest 18·7 mgm. per lb. per day. Patients who responded to the lowest doses were kept at that level. Those who developed inflammatory reactions or who showed little response after 2–3 weeks received larger doses. It was found that, irrespective of the size of the dose, a minimum of 21–28 days was required for the outgrowth of normal hair as observed by Wood's light. Cultures were not made until the third to fifth week when the distal parts of the hair which were fluorescent could be clipped off. It was found that culture positive material was present for several weeks after the disappearance of the fluorescent material. In some cases fluorescent material reappeared in the originally infected sites. In 3 cases where the lesions had cleared to the extent of giving a first negative culture there was relapse. Subsequently, therefore, treatment was prolonged until 2 successive cultures 1 week apart were negative. After 2 weeks these patients were examined further and scales and hair stubs cultured. After a further month, if the lesions remained negative, the patient was discharged. In the case of patients with *Trichophyton tonsurans* infection where fluorescence by Wood's light was absent a series of cultures was made 21–28 days after treatment had commenced. By this time scaling had subsided and normal hair was making its appearance. Patients were discharged after 3 negative cultures spaced over a month were obtained.

The results of treatment are given in the case of 81 of these patients. 70 of the patients presented with lesions due to *Microsporum audouini*. At 70 days after the commencement of treatment overall results irrespective of dosage showed that 64 were Wood's light negative, and 48 were culture negative. 16 were culture positive for 70 days and longer. The individual response varied considerably. Thus, apparent cures were obtained with doses of only 250 mgm. per day for 7–14 days, while in 2 cases positive cultures were still being obtained after 77 days of continuous treatment with 750 mgm. per day. However, it appears that patients who received a dose of at least 10 mgm. per lb. per day showed the best response. Some other factors influencing the nature of the patients' response to treatment were observed, for example, patients suffering from tinea capitis for more than 1 year appeared to respond more rapidly than those in whom the infection had been present for less than 2 months, and patients with minimal infection responded more rapidly than those with extensive infection. 4 patients presenting with *M. canis* infection were Wood's light negative by the 35th day after commencement of treatment with a daily dosage of 10·6 to 14·5 mgm. per lb. 1 of the patients was culture negative at 56 days. The subsequent course of events in these cases varied considerably. Another patient with *M. canis* infection relapsed, but cure followed when the dosage was increased. 6 patients with *T. tonsurans* infection were clinically cured by doses varying from 4·7 to 10·9 mgm./lb. daily. *C. J. La Touche*

MULLINS, J. F., JAMPOLSKY, N. A. & PINKERTON, Mary E. **Oral Treatment of Superficial Mycoses with Griseofulvin.** *Texas Reports on Biol. & Med.* 1959, v. 17, No. 3, 411–22, 6 figs.

Yet another of the many successful therapeutic trials with the valuable oral antifungal drug griseofulvin [see this *Bulletin*, 1959, v. 34, 335, 894] is described here by the authors. The results of treatment of 24 patients are recorded. Adults received 1 gm. by mouth daily and children 14 mgm./kgm. These patients presented with lesions in a variety of sites such as the buttocks, the groin, the nails, or generally distributed (all of these due to infection by *Trichophyton rubrum*) and the lesions of the scalp (due to infection by *T. tonsurans* or *Microsporum audouini*).

The first beneficial effect was relief from pruritus in 8 patients suffering from *T. rubrum* infection who had experienced this distressing symptom before the administration of this drug. In fact, in these patients it ceased on the 3rd or 4th day after treatment began. Cultures from lesions due to *T. rubrum* were negative in 1 to 3 weeks, exclusive of onychomycosis, and in 4 to 5 weeks in *M. audouini* and *T. tonsurans* infections of the scalp. Scrapings from these lesions were microscopically positive for some time after they had become culturally negative. *T. rubrum* lesions of the smooth skin were clinically clear in 9 patients after 2 to 7 weeks' therapy and in the case of onychomycosis there were at least signs of normal nail growth after 5½ weeks' treatment. Tinea capitis lesions were clinically clear, or at least showed normal hair growth, after 5 to 8 weeks' treatment.

Only a few of the patients did not respond to treatment with this drug or responded only slightly to it; in 1 case of *T. rubrum* infection (groin and buttock lesions) there was recurrence of infection. Undesirable side effects such as headache, hypertension and granulocytopenia were observed in isolated instances and were only temporary. The duration of the *T. rubrum* infections before treatment with this drug was from 1 to 36 years, and *T. tonsurans* and *M. audouini* from 6 to 17 months. *C. J. La Touche*

VICHER, E. E., LYON, I. & WHITE, E. L. **Studies on the Respiration of** *Trichophyton rubrum*. *Mycopathologia*. The Hague. 1959, Oct. 15, v. 11, No. 3, 185–95, 1 fig. [18 refs.]

SALVIN, S. B. & SMITH, R. F. with the technical assistance of Aspascia COBURE & Jane NISHIO. **Antigens from the Yeast Phase of** *Histoplasma capsulatum*. **III. Isolation, Properties, and Activity of a Protein-Carbohydrate Complex.** *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 45–53, 4 figs. [17 refs.]

"A purified antigen from the yeast phase of *Histoplasma capsulatum* was prepared from the broth in which the cells had been grown and been permitted to autolyze. This component was active in inducing delayed type reactions in sensitized guineapigs and humans. It also was capable of increasing the resistance of mice to lethal challenge. Physico-chemical analysis indicated it to be a complex containing carbohydrate and protein moieties."

FARID, Z. & BARCLAY, W. R. **Histoplasmosis. *In vivo* Studies in the Rabbit Ear Chamber.** *Arch. Pathology*. 1959, Oct., v. 68, No. 4, 413–18, 8 figs.

The authors describe the microscopical features which they observed in lesions experimentally induced in a rabbit's ear with spores of *Histoplasma capsulatum*. Their observations were made through a simplified rabbit ear chamber which is described by them in an accompanying article.

Inoculation was effected by depositing on the surface of the vascularized connective tissue of the rabbit's ear a small number of spores.

Within 1 hours of the inoculation leucocytes could be seen adhering to the vascular endothelium. At 2–3 hours after inoculation extravasation of white cells took place. These white cells then moved towards the spores and an hour later the spores were surrounded by them. At first the leucocytes appeared to be repelled by the spores. Extravasation of serum and leucocytes continued during the next 2 days. By the 6th day a few of the spores were seen inside the macrophages, but the majority were merely surrounded by them. During the 2nd week the spore contents began to shrink or become segmented. Disintegration of the spore walls followed and yeast phase cells were liberated. By the 9th day there were many empty spores with fractured walls. At this time there was a second inflammatory reaction thought to be coincident with the liberation of yeast cells from the spores. Finally, the vessels in the immediate area containing the spores became thrombosed and by the 3rd week the whole area became involved in a necrotic process with abscess formation.

Response to secondary infection with *H. capsulatum* broadly speaking, resembled that which was associated with primary infection. It differed mainly in that it "did not subside but continued to grow in intensity and extent during the first week of the infection". By the 5th day the inoculation site had become avascular, densely packed with inflammatory cells and surrounded by grossly dilated, tortuous blood vessels. The inflammatory reaction began to subside from the 10th day onwards, and the inoculation site became gradually revascularized and underwent complete resolution. 6 months after this secondary lesion had healed there was no recrudescence of the infection even though spores could be discerned in the area for 1 month after inoculation. *C. J. La Touche*

WIDRA, A. **Studies on the Nucleus of** *Candida* **spp.** *Mycopathologia*. The Hague. 1959, Oct. 15, v. 11, No. 3, 177–84, 20 figs. [23 refs.]

HASENCLEVER, H. F. **Comparative Pathogenicity of** *Candida albicans* **for Mice and Rabbits.** *J. Bacteriology*. 1959, July, v. 78, No. 1, 105–9.

This work was undertaken with a view to determining the relative pathogenicity of *Candida albicans* in the

Swiss white mouse and the albino rabbit on a weight for weight basis. Average weight determinations were made before inoculation. The LD50 was determined for each strain of *C. albicans* by the method of Reed and Muench but with the modification that the calculated LD50 was divided by the average weight of the groups of mice or rabbits receiving the various dilutions of the same strain. For example, when the LD50 in mice was $8{\cdot}9 \times 10^4$ the average weight of the mice used for this strain was 19·4 gm. therefore, the LD50 per gm. was $8{\cdot}9 \times 10^4/19{\cdot}4$ or $4{\cdot}6 \times 10^3$ yeast cells. In the case of the rabbits the LD50 was divided by 1850 gm. the average weight of 8 rabbits.

Results indicated considerable variation in pathogenicity for different strains. Thus, strain 50 was highly pathogenic for both mice and rabbits, whereas strains B 311 and 3162 were more lethal for mice than for rabbits. The least pathogenic strain for both mice and rabbits was strain 857. None of the other species of *Candida* except *C. tropicalis* was lethal for mice. In the case of the rabbits none of the other species of *Candida*, namely *C. parapsilosis*, *C. stellatoidea* and *C. tropicalis*, was lethal. Most of the strains of *C. albicans* were able to produce a progressive disseminated disease in the mice and positive cultures were obtained from the liver, spleen and kidney. In mice these organs showed the most striking gross changes, including large abscesses in the kidneys. In the case of mice which died as a result of infection by *C. tropicalis* positive cultures were obtained from the brain, lung, liver, spleen and kidney. The course of the disease was more acute in rabbits than in mice, death occurring in from 1 to 7 days after inoculation. A further experiment in which only mice were used was carried out to provide a more quantitative procedure. Three strains of *C. albicans* were used while 6 groups of mice were inoculated with each strain.

From the results obtained it is concluded that mice are at least as susceptible if not more susceptible to candidiasis than are rabbits and that the size of the inoculum is of great importance in comparative virulence studies in 2 animal species varying 100-fold in weight.

*C. J. La Touche*

BRAUDE, A. I. & ROCK, J. A. **The Syndrome of Acute Disseminated Moniliasis in Adults.** *Arch. Intern. Med.* 1959, July, v. 104, No. 1, 91–100, 7 figs. [29 refs.]

Systemic mycotic infection in adults generally reflects a lowering of the body's forces of resistance. The cases which have so far been recorded in the literature provide ample illustration of this. In the light of these records and of a further case of systemic moniliasis which they describe, the authors of this paper have attempted to determine what disturbances in resistance are responsible for this type of infection in adults and to define the clinical syndrome of systemic moniliasis in these patients.

The clinical course of an illness in a male patient aged 55 years is described in detail from its sudden onset to its rapid and fatal termination. Surgical intervention to correct an intestinal abnormality was complicated by an accidental injury to the ileum. Antibiotic therapy failed to check the rapid decline in the patient's condition after this operation. Laboratory investigations during the terminal phase of the patient's illness revealed the presence of *Candida albicans* in the bloodstream in overwhelming quantity, and also in the urine. At autopsy, findings included multiple abscesses in the kidneys, heart, thyroid, brain, pancreas, adrenals and liver, and, what was probably of great significance, an ulcer in the ileum.

The authors conclude from a study of this case and the records of others that the lowering of the body's resistance to infection by *C. albicans* is related to: (1) alteration in the bacterial flora of the bowel due to prolonged antibiotic treatment, and (2) injury to the gastrointestinal mucosa; and define the syndrome of acute disseminated moniliasis in adults as a clinical entity in which there is (1) a background of continuous antibiotic treatment during the course of a protracted debilitating illness, and (2) an abrupt decline in the clinical course, with the development of fever, shock, depressed sensorium and gastrointestinal bleeding.

*C. J. La Touche*

GRAHAM, Rosemary D. **Oral Thrush in Infancy treated with Nystatin.** *Lancet.* 1959, Oct. 17, 600–601.

The results of a comparative clinical trial between the therapeutic efficacy of nystatin and 1% aqueous gentian violet in 55 infants suffering from oral thrush are described. All but 2 of the infants were otherwise healthy. 26 were treated with 1% aqueous gentian violet applied to the oral mucosa with a cottonwool swab twice daily, while 29 received 1 ml. of nystatin suspension 4 times daily dropped into the mouth after the feeds.

Of the 26 infants treated with gentian violet 16 responded within 14 days, whereas of the 29 infants treated with nystatin 28 responded within 14 days. There was no response in 4 patients treated with gentian violet and 3 so treated relapsed. Only 1 patient treated with nystatin relapsed.

Mothers preferred to administer nystatin rather than gentian violet because it did not stain. In the author's opinion the therapeutic advantages of nystatin over gentian violet are that it is non-toxic and non-irritating and does not stimulate allergic responses. Its one disadvantage is its cost (about 10 shillings per week of therapy as against a few pence in the case of gentian violet).

*C. J. La Touche*

LONES, G. W. & PEACOCK, C. L. **Alterations in *Candida albicans* during Growth in the Presence of Amphotericin B.** *Antibiotics & Chemotherapy.* New York. 1959, Sept., v. 9, No. 9, 535–40, 3 figs.

"Twelve strains of *Candida albicans* were grown for 52 serial transfers in culture media containing graded concentrations of amphotericin B added as a sodium desoxycholate complex. All strains experienced an increased tolerance for the antibiotic. Although in most strains the change was small, in three of the strains the increase in the concentration of antibiotic

required for 50 per cent inhibition of growth was tenfold or greater. Other alterations were noted in varying degrees in the derived strains. Decreased ability to form mycelium and chlamydospores and decreased growth rates were observed. The two derived strains having the greatest tolerance for amphotericin B were found to have a markedly decreased virulence for mice."

KUBISTA, R. A. & DERSE, P. H. **A Comparison of Triacetin and Nystatin with respect to their Stability and Effect on** *Candida albicans*. *Antibiotics & Chemotherapy*. New York. 1959, Sept., v. 9, No. 9, 546–9, 1 fig.

"A comparison of triacetin and nystatin was undertaken to determine the effect of blood serum upon each fungistatic agent and to determine the extent to which resistant cultures of *Candida albicans* might be expected to appear. The stability of both agents was measured.

"The results indicate that triacetin is more stable, enhanced by blood serum, and not likely to give rise to resistant cultures after prolonged periods of exposure."

LITTMAN, M. L. & TSUBURA, E. **Effect of Degree of Encapsulation upon Virulence of** *Cryptococcus neoformans*. *Proc. Soc. Exper. Biol. & Med.* 1959, Aug.–Sept. v. 101, No. 4, 773–7, 2 figs.

"Thinly encapsulated *cryptococcus neoformans* cells were equally as virulent for white Swiss mice as thickly encapsulated cells of the same strain. Yeast cells initially possessing thin capsules promptly developed thick ones upon intracerebral injection into mice, and upon subculture to synthetic capsule medium. Both types of cells produced hydrocephalus to an equal degree. Degree of encapsulation is not a factor in virulence of *Cryptococcus neoformans* for white Swiss mice."

LATAPÍ, F., LAVALLE, P., NOVALES, Josefa & ORTIZ, Yolanda. Griseofulvina en Micosis Cutáneas Profundas. Nota preliminar sobre resultados terapéuticos en un caso de Micetoma por N. brasiliensis y un uno de Esporotricosis por S. schenckii. **[Griseofulvin in Deep Cutaneous Mycosis. Preliminary Note on Therapeutic Results in a Case of Mycetoma due to** *Nocardia brasiliensis* **and one of Sporotrichosis due to** *Sporotrichum Schenkii*. *Dermatología*. Mexico. 1959, Jan.–Mar., v. 3, No. 1, 34–41, 8 figs [16 refs.]

The English summary appended to the paper is as follows:—

"Griseofulvin, the new antibiotic which has been obtained from 'penicillium griseofulvum' has been found useful against several skin conditions produced by dermatophytes. Recent literature is reviewed and good results are reported too by the authors.

"From the special studies they have started in Mexico on griseofulvin treatment of deep mycoses, a preliminary optimistic report is given on the action of the new drug in two cases, one of Mycetoma by Nocardia brasiliensis, and the other one of Sporotrichosis. They insist, however, that a final conclusion is not possible at the present time."

SMITH, Marthe E., BURNHAM, D. K. & BLACK, M. B. **Cerebral Mucormycosis. Report of a case.** *Arch. Pathology*. 1958, Oct., v. 66, No. 4, 468–73, 7 figs. [15 refs.]

This almost invariably fatal disease, though apparently of rare occurrence in the past, is now being recorded with ever-increasing frequency. When it occurs it is usually as a complication of diabetes and the case described here is no exception.

The patient was a diabetic aged 38 years with a family history of diabetes. He had been admitted to hospital for control of his diabetes in December 1956. At this time, apart from his diabetic syndrome, the outstanding clinical features of his case were arterial hypertension and optical lesions. These features were described by the ophthalmologist who attended the patient in the following words (quoted by the author): "Old retinal tear with choroiditis of the left eye, mild diabetic retinopathy, and recent acute vascular hypertensive changes".

When the patient was discharged the "Discharge Diagnosis" was as follows: "Diabetes mellitus, labile type, possible Kimmelstiel-Wilson kidney and (?) subacute glomerulonephritis with arterial hypertension".

He was readmitted on 4 September 1957 in coma with a recent history (obtained from his physician) of "sinusitis, with stuffiness in his nose, and fever. X-rays of the sinuses were reported to have shown some clouding. He was given antibiotics, but became rapidly worse. Three days later swelling of the right eye and eyelid was noted. He was given a blood transfusion. Fever continued high, and he developed difficulty in urinating, became comatose and was transferred to St. Luke's Hospital by ambulance". The clinical diagnosis made on this occasion was: "Labile diabetes, subacute glomerulonephritis, and cavernous sinus thrombosis".

The clinical course was of short duration. Rapid deterioration set in despite antibiotic therapy, intravenous fluids and artificial respiration, and the patient died 36 hours after he was admitted. During this time laboratory investigations included blood cultures and cerebrospinal fluid cultures. These were negative, but the cerebrospinal fluid contained 89 white blood cells and 32,250 red blood cells per cmm. and the blood count showed 37,000 white blood cells.

At autopsy "the entire upper face was edematous. Nasal and mouth passageways contained thin bloody fluid. . . . The edematous brain (1380 gm.) demonstrated a bulging right hemisphere and a cerebellar pressure cone. Almost the entire right temporal lobe was replaced by clotted blood . . . which protruded from the lateral surface and displaced the right basal ganglia medially. Subarachnoid hemorrhage was limited to the right temporal lobe surface. . . . The sphenoid sinus contained mucopurulent material. . . ."

Microscopical findings included the presence of tangled masses of broad, branching, non-septate hyphae in unorganized thrombi in both internal carotid arteries and in their muscularis layer. These occurred also in the cavernous sinus.

Although cultures were made from the sphenoid sinus and from the cerebrospinal fluid at autopsy only *Staphylococcus* was grown. Cultures for fungi were not made either ante mortem or post mortem. The diagnosis of cerebral mucormycosis rested therefore solely on the post mortem microscopical findings. However, since the terminal clinical picture included features so characteristic of cerebral mucormycosis (when considered in the context of a diabetic syndrome) a provisional diagnosis of cerebral mucormycosis would have been justifiable on clinical grounds alone.

[See also this *Bulletin*, 1957, v. 32, 666.]

*C. J. La Touche*

# Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

*For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the* TROPICAL DISEASES BULLETIN.

## TUBERCULOSIS

HUSTON, A. F. & EDWARDS, C. O. **Tuberculosis in the Family.** *Brit. Med. J.* 1959, Oct. 24, 798–801.

This paper describes the type of tuberculosis seen in 87 children under 14 years of age in a paediatric department in southern England in 1951–58.

There were 62 cases of primary and 25 cases of disseminated disease:

| Primary Disease (62 Cases) | | Disseminated Disease (25 Cases) | |
|---|---|---|---|
| Bronchial adenitis only | 27 | Meningitis only .. .. | 10 |
| „ „ with segmental collapse .. | 11 | „ with miliary | 4 |
| Pleural effusion .. .. | 9 | Miliary only .. .. | 2 |
| Cervical adenitis .. | 7 | Bone and joint .. .. | 6 |
| Abdominal „ .. .. | 3 | Renal .. .. .. | 1 |
| Cutaneous .. .. | 2 | Adult-type pulmonary .. | 2 |
| Aged 3 and under with positive tuberculin test | 3 | | |

Tuberculosis in childhood may be diagnosed because of suspicious symptoms in a child or by examination of child contacts of tuberculous adults. The diagnosis in these 87 patients was made by the hospital physician in 64 (39 primary and 25 disseminated) and at the chest clinic in 23 (all primary).

The clinical features were so varied as to cover the whole field of medical or surgical diagnosis among children. The early diagnosis of tuberculous meningitis provided the most urgent problems. It was present in 14 children while 19 others required lumbar puncture to exclude the diagnosis.

Tuberculin testing was considered to play an important part in diagnosis; all the children in the series were reactors.

A probable source of infection was found for 74 children, and none was discovered for the other 13. The sources of infection were:

| | Father | Mother | Grand-parents | Uncles/ Aunts | Siblings | Others | Milk | Total |
|---|---|---|---|---|---|---|---|---|
| Probable infecting contact .. | 20 | 9 | 10 | 8 | 2 | 10 | – | 59 |
| Known sputum-positive .. | 17 | 8 | 8 | 6 | 1 | 6 | – | 46 |
| No. of children infected .. | 26 | 10 | 11 | 9 | 2 | 10 | 6 | 74 |

Extra-familial sources of human infection included a landlady, dwellers in the same block of flats and a greengrocer. There was no discovered instance of school infection. Milk-borne infection occurred in 5 children in 1951–52 and in one in 1954.

During the period of observation chemotherapy, BCG vaccination, the abolition of waiting lists for sanatoria and the specific treatment of primary disease were important factors in the control of infection, and seem to have met with considerable success.

X-ray examination of suspected adults revealed 7 previously unknown cases of pulmonary tuberculosis (6 sputum-positive). An example is given of the discovery of advanced pulmonary tuberculosis with cavitation in the father of an infected infant. He had never attended a chest clinic or had specific chemotherapy but the tubercle bacilli iso'ated from his sputum and those from the child's cerebrospinal fluid were resistant to isoniazid and partially resistant to streptomycin.

For the paediatrician tuberculosis remains a serious clinical problem and for the chest physician a tuberculous child indicates an infector. Infectors must be found and treated and BCG vaccination offered to all children and adolescents likely to be in contact with tuberculous infection. *H. G. Calwell*

MARCHAND, M., TISON, F. & GLORIAN, P. A propos de 211 dépistages de tuberculose évolutive en milieu industriel. [**Active Pulmonary Tuberculosis in Textile Workers in France**] *Arch. Malad. Professionnelles.* Paris. 1959, May–June, v. 20, No. 3, 314–16.

The industrial medical service concerned in this survey covers 115,000 workers mostly engaged in the textile industry. Compulsory periodical X-ray examination of the chest is done in static radiography units in factories possessing them or in mobile units or in a radiography centre.

The total number of workers X-rayed at one centre in 1957 was 60,907 of whom 211 were found to have active pulmonary tuberculosis (3·5 per 1,000). In addition 138 persons known to have pulmonary tuberculosis were kept under observation.

The forms of the disease seen were:

| | | |
|---|---|---|
| Minimal lesions, early and unilateral ... | 90 | (42%) |
| Moderately advanced lesions ... ... | 70 | (33%) |
| Advanced lesions with cavitation ... ... | 40 | (20%) |
| Far advanced lesions ... ... ... | 11 | (5%) |

The disease was bilateral in 55 persons (26%), and there was evidence of reactivation of previous stabilized lesions in 10 cases.

On clinico-radiological grounds it was concluded that the cases fell into the following groups:

| | | |
|---|---|---|
| Complications of primary infection ... | 4 | |
| Pleurisy and its complications ... ... | 9 | |
| Nodular lesions ... ... ... ... | 55 | |
| Infiltrative lesions without visible cavitation ... ... ... ... | 92 | |
| Cavitation ... ... ... ... | 51 | (24%) |

Workers found to have active tuberculosis are sent from work and referred for treatment to their doctors. Their condition is reviewed in due course to see what work they are fit for (whether full- or part-time) or what rehabilitation is needed.

Records of the whole medical service of the group show that in 1957 the total number of cases of active pulmonary tuberculosis discovered was 560 and in the previous 10 years the total number was almost 5,000. Some 75% of patients had early lesions which could be cured quickly, but in the others the disease was advanced. In such cases the patient may not have been employed previously or may not have been X-rayed because of deficient medical service but usually the disease has developed rapidly between 2 annual X-ray examinations.

The authors concluded that there was no decline in the incidence of pulmonary tuberculosis or of its severity in their region. *H. G. Calwell*

TSUJI, S. [**Tuberculosis of Employees in Small and Medium Enterprises.**] *Igaku Kenkyu.* Fukuoka. 1959, Aug., v. 29, No. 8, 2749–63, 12 figs. [55 refs.] [In Japanese.] [English summary.]

In the period 1952–58 the author examined 12,611 males and 2,671 females in about 400 factories, mostly by X-ray. Small factories had on the whole more young employees than large factories.

4–5% showed active tuberculosis, 1% needing treatment. The rate in employees who at first avoided examination and were later examined compulsorily was very high—25%.

The author concludes that tuberculosis is much more prevalent in employees of small and medium enterprises than in large organizations, and much more attention should therefore be paid to these small communities. *Charles Wilcocks*

ROYAL NETHERLANDS TUBERCULOSIS ASS. **The Tuberculosis Clinic. Some of its Working Methods and their Efficacy.** [GRIEP, W. A.] *Proc. Tuberculosis Res. Counc.* 1958, No. 45, 5–39, 1 fig.

This interesting paper asks and tries to answer the question: "Does the diminution in the morbidity and mortality arising from the use of antimicrobial drugs call for a change in the procedure at present in vogue at tuberculosis clinics?" Taking the notified cases throughout Holland, comparison is made of the methods used at the clinics in 1952 and 1956. Although the total is halved no striking percentage difference is found. A fall in the percentage of patients sent by family doctors is largely balanced by a percentage increase of those sent by specialists. The percentage discovered by mass X-ray surveys was about 18 in both years. The fall in numbers, however, has meant that now 2,000 persons have to be X-rayed to find one active case of tuberculosis.

Of patients considered to have inactive lesions at the first examination, 1% had relapses during the first 3 years of observation but relapses were relatively rare subsequently. Relapses both of cases apparently successfully treated and those considered inactive were commoner in younger people. Regular appointments should be given to these patients; it should not be left to the patients to come up if they feel any suspicious symptoms.

Contact examination was fruitful at the first examination (2·5% had active disease) but subsequent examination only produced 0·2%. Contact examination showed that infection from family sources was much less where the patient was aware of the diagnosis or had been trained in a sanatorium. Some cases are missed because the tuberculin reaction had not developed when the test was made. Negative Mantoux tests on contacts should be repeated at the end of 6 months. The risk of developing tuberculosis was much greater when the infection was contracted during adolescence; and when the reaction to tuberculin was strong.

Although it is not specifically stated the author appears

to think that little change is required in tuberculosis clinic procedure, but all healthy negative reactors must be regularly Mantoux tested until adult life is reached. Many other aspects are ably discussed. 27 elaborate tables are appended showing the figures on which the conclusions are based.

[This is a piece of constructive work of considerable value.] *F. H. Young*

ROYAL NETHERLANDS TUBERCULOSIS ASS. **A Population Survey in a Community with a High Tuberculosis Incidence. Notes on Field Observations** [HUISKEN, D. P. & BLEIKER, M. A.] *Proc. Tuberculosis Res. Counc.* 1958, No. 45, 50–56, 3 figs.

During the years 1954–56 an unusually large number of cases of pulmonary tuberculosis were notified from the Dutch village of H., in a rural area. In view of this a combined X-ray and tuberculin test survey was carried out in May 1957. Of the 2,392 inhabitants over 1 year of age, 2,335 (97·6%) were X-rayed; 2,312 persons were tuberculin tested and 2,205 of the tests were read. 2 active and 11 inactive cases were brought to light by the X-ray examinations. As regards the tuberculin tests an induration of 6 mm. read after 72 hours was regarded as positive to 5 units of PPD.

Tables are given of the results in males and females. In both the percentage of positive cases was only about 30% in the age-group 21–24 years. It then rose rapidly to about 65% in both sexes. After this the percentage rose to about 80% in males and 70% in females, falling a little in old age. After the survey no cases of pulmonary tuberculosis, but 3 cases of extra-pulmonary tuberculosis, were notified during the remainder of the year.

The combined survey was repeated in May 1958. No new cases were found, but 14 persons had converted their tuberculin test. Despite these surveys, 3 new cases were found in the remaining 7 months of the year. *F. H. Young*

ROYAL NETHERLANDS TUBERCULOSIS ASS. **The Problems of Relapse in Pulmonary Tuberculosis** [EDENS, J. D.] *Proc. Tuberculosis Res. Counc.* 1958, No. 45, 57–96. [15 refs.]

In Holland during the past few years a static 30% of the patients with non-primary active diseases are relapse cases. This paper deals with the frequency and causes of relapse. After a review of the literature the author considers the relapses at the Philips tuberculosis clinic. Relapse is defined as the reappearance of active pulmonary tuberculosis more than 3 months after clinical recovery, and requiring treatment. The study is restricted to relapses within 3–4 years after treatment and considers 641 relapses. An occasional positive sputum without further evidence of activity is excluded.

Five 4- or 5-year periods 1936–39 to 1953–56 are taken, and the proportion of new cases to relapses were 2:1, 3:1, 2·5:1, 2:1, and 1·5:1, though the number of new cases was falling rapidly in the last two periods —184 and 99. Elaborate statistical tables are appended and show the following results.

1. The incidence of relapse has fallen from 31% in the first period to 14% in the penultimate period.
2. Most relapses take place in the first two post-treatment years. This has not changed.
3. Little difference is noted between cases with large and cases with small lesions originally, or cases originally positive and those negative. This is not in agreement with the results obtained by most authors.
4. Age and sex, or home or sanatorium treatment, or the methods leading to diagnosis, had little effect.
5. Those who returned to work immediately had a lower relapse rate than whose who did not.
6. The main adverse factor is the lack of induration in the residual lesions, especially if associated with a heavily positive sputum before treatment.

The author coins the term "healing tendency", which collates the original lesion with the residual lesion. As antimicrobial treatment reduces the size of the residual lesion, a decrease in the relapse rate may be looked for.

[This is an interesting paper in that its conclusions are not altogether in line with those of many other authors, though little exception can be taken to the way the material is handled.] *F. H. Young*

EILERTSEN, E. **Epidemics of Primary Tuberculosis and their Significance.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, No. 3, 203–16, 1 map. [23 refs.]

The tuberculosis situation in the city of Bergen, Norway (population 113,000 and 50,000 in the suburbs), has vastly improved in the past two decades. The death rate was 7·9 per 100,000 in 1955, the incidence of destructive pulmonary tuberculosis had fallen from 119 per 100,000 in 1940 to 44 in 1955, and the tuberculin reactor rate at the age of 7 years from 6·3% to 1·4%. The rates at 14 years of age were 14·8% and 6·3% respectively.

In 1956 there was an outbreak of 48 cases of primary tuberculosis in an area of the city where housing and living standards were above the average. During 10 days in mid-June 3 children were admitted to hospital with primary tuberculosis. Examination of their family and household contacts failed to reveal a source of infection, and as the children were living in the same small group of houses it was assumed that there must be a common source of infection outside their homes.

During the course of the investigation several more children aged 6–14 years in the vicinity were found to have primary tuberculosis.

Within 3 months of the diagnosis of the first case the whole school population, about 3,000, had been tested with tuberculin anew and X-rayed where necessary. In addition 10,963 persons out of a total of 12,002 in the area had been tested and X-rayed. The majority of the absentees were away at sea.

The survey discovered a total of 42 persons in whom tuberculin conversion indicated infection within the previous 6 months; 25 of these had symptoms due to infection and 13 were admitted to hospital. All 42 lived in the same group of houses as the original children but all were from different households.

During the investigation attention was directed to the shopping centre and a woman aged 38 years, who dealt in pasteurized milk in sealed bottles, was found to have active pulmonary tuberculosis with cavitation and a positive sputum. She was admitted to hospital within a few days of the occurrence of the first 4 cases.

This woman had been X-rayed in 1955 as a condition of employment and found to have a minimal tuberculous lesion which was considered then and at 6 subsequent examinations to be inactive. She had been unwell with cough and pain in the chest but had continued working for about 2 months during which many customers, mostly children, had been in contact with her 4–6 times a week. Further investigation showed that she had infected 6 other young persons elsewhere during short periods of more occasional contact.

All of the 42 who had been infected in the shop were known to have been non-reactors shortly before exposure and were thus able to act as indicators of infection. Young children formed the predominantly susceptible group, as in Bergen less than 5% of children under 14 years are vaccinated routinely with BCG whereas nearly all over that age have been vaccinated or have contracted natural infection before vaccination.

Many examples of outbreaks of tuberculosis are quoted from the literature, the factors which influence the spread of infection are discussed, and it is emphasized that the significance of the individual infectious patient becomes greater as the non-immune part of the population increases in number owing to improved control of tuberculosis. [The work described is an example *par excellence* of tuberculosis control.]

*H. G. Calwell*

PLESSIS, J., DUCLOUX, M., GENTILLINI, M. & SANKALÉ, M. La tuberculose en zone sahelo-saharienne (Cercle de Gao-Republique, Soudanaise). **[Tuberculosis in the Gao Area, Soudan, West Africa]** *Méd. Afrique Noire.* Dakar. 1959, Aug 16–31, v. 6, No. 16, 365–68, 1 map & 9 figs. [14 refs.]

The area of Gao in Soudan, West Africa, has been neglected from the point of view of tuberculosis until very recently. In June 1957 Gao received its first X-ray equipment; 137 new cases were discovered; of these 96 occurred in dwellers in villages and 41 in nomadic people. Many of the farmers go to Ghana in search of work.

The characteristics of the two groups are described. Clinically the disease is often very acute, toxic, and far advanced; large cavities are frequent. Skeletal forms are very common, and are supposedly due to bovine infection.

Treatment by drugs follows orthodox lines as far as is practicable under the circumstances; reaction to treatment is similar to that experienced in other centres. No major surgery is being done.

A review of the way in which the disease can be reduced is given. A control of the immigrants returning from work in Ghana is thought to be essential.

*F. H. Young*

BRUNEL, M. La tuberculose pulmonaire au Cameroun en 1958, endémie tuberculeuse, formes cliniques, traitement, prophylaxie. **[The Manifestations, Treatment and Prophylaxis of Pulmonary Tuberculosis in the French Cameroons]** *Bull. Soc. Path. Exot.* 1958, Nov.–Dec., v. 51, No. 6, 920–35, 1 map & 1 graph.

HOUPEAU as the result of a survey made in 1950 [this *Bulletin*, 1954, v. 29, 1144] concluded that tuberculosis had become a serious public health problem in the French Cameroons and that the disease was spreading. The author presents an account of the problem in 1958.

The first systematic tuberculin survey was made in 1955, since when 330,154 tests have been done (Mantoux 10 TU). Surveys have been confined mostly to pre-school children and adolescents. The mean reactor rate as reported in some early studies of 1932–33 was 18·8%; in 1955 it was 25% and in 1956 and 1957 about 33%.

Reactor rates were highest in the most populous areas where industrial development was prominent, and lowest in remote and sparsely populated areas. Racial and climatic factors were found to have little influence. Surveys made in 1956–58 showed that the mean reactor rate rose from 13·5% at 0–4 years to 56·9% at 16–20 years. There was a sharp rise between 6 and 8 years and again between 12 and 15 years. Otherwise the rise was steady.

Although diagnostic centres are insufficient in numbers their findings present an estimate of the amount of tuberculosis in the territory. In 1932–33, 198 cases were reported (6 per 100,000), in 1955, 853 (26), in 1956, 1,168 (37), and in 1957, 1,202 (40). The increase is due partly to better facilities for diagnosis and partly to spread of the disease. Urban centres were the worst affected, and the highest incidence was at 20–30 years. Males are more often affected than females in the proportion of 69% to 31%. [It is not stated what their proportions in the population are or whether they attend for examination in proportionately equal numbers.] Racial factors were not found to play an important part in morbidity.

The clinical forms of the disease seen in an urban tuberculosis centre of 205 beds since 1951 were recorded. In 1958 there were 1,417 patients on the register of whom 1,206 had pulmonary tuberculosis, 191 primary lesions, 11 tuberculous adenitis, 3 meningitis, 5 spinal disease and 1 renal disease. Nearly all had sought advice because of illness and all were of the poorer class—daily workers, domestic servants or minor civil servants.

The pulmonary tuberculosis was bilateral in 70·1% (extensively cavitated in 45·9%) and unilateral in 27·9% (extensively cavitated in 15%). The high proportion of extensive disease is attributed to ignorance and neglect. Many patients are unable to stop work because of consequent hardship in the home. Some had already undergone half-hearted treatment at the hands of private doctors while remaining at work.

Hospital treatment is always advised; shortage of beds limits the stay of patients with advanced disease to

10 months and of others to 3–6 months but chemotherapy is continued after discharge. A combination of 2 or 3 drugs is used. Collapse therapy has almost disappeared.

It was possible to follow up only 329 of the 1,206 patients treated in the period 1951 to mid-1958. 254 (77·1%) were completely cured and 75 (22·9%) not cured, of whom 45 who were improved but intermittently infectious could have been cured by operation and 30 had failed to respond to treatment.

In the prevailing situation the need is for the extension of BCG vaccination, for mass radiography and for the provision of more tuberculosis dispensaries to undertake the ambulatory treatment and supervision of patients. *H. G. Calwell*

COMSTOCK, G. W & PORTER, Merilys E. **Tuberculin Sensitivity and Tuberculosis among Natives of the Lower Yukon.** *Pub. Health Rep.* Wash. 1959, July, v. 74, No. 7, 621–34, 7 figs. [25 refs.]

The prevalence of tuberculosis is very high among the indigenous people of Alaska but little is known of its epidemiology. A tuberculin survey was made in 1957 in an area of the Yukon in order to obtain information about the prevalence of infection as a controlled trial of isoniazid prophylaxis was about to be initiated.

The work was done by 3 experienced public health nurses. The Mantoux test was used with 5 TU of PPD-S and reactions were examined on the 2nd day (occasionally on the 3rd day); the diameters of erythema and induration were measured and recorded.

The study population consisted of 2,211 persons from 19 villages of whom 1,777 were classified as Eskimos, 429 Indian and 5 mixed Eskimo and Indian. Many of each race have some admixture of white blood.

Consideration was given to the possibility of non-specific tuberculin sensitivity affecting the results but the evidence available supported the view that natural sources of non-specific sensitivity are not common in Alaska. It was expected that there would be some sensitivity due to previous BCG vaccination in younger persons and care was taken to identify those already vaccinated. Some persons already vaccinated may have nevertheless been classified as unvaccinated but the degree of error in this regard was small.

In addition to PPD-S 301 persons in the group were given 5 TU of PPD prepared from an organism resembling a mycobacterium (PPD-C). Of the 179 persons who reacted to both antigens only 1 had a significantly larger reaction to PPD-C than to PPD-S. This and other findings suggest that the kind of non-specific sensitivity detectable by PPD-S is uncommon in the study population.

It was considered reasonable to estimate the prevalence of tuberculous infection on reactions of 5 mm. or more as BCG vaccination in this population had resulted in a low degree of sensitivity. By this criterion the reactor rate was 22% at 0–4 years and 96% at 15–19 years which high rate was maintained to 65 years with a moderate fall thereafter.

The average annual infection rate was estimated at 15% but it appeared likely that the rate 20 years earlier was appreciably higher than 15% and that more recently it has fallen to (possibly) 5%.

Among unvaccinated adult reactors the prevalence of active and inactive reinfection type pulmonary tuberculosis was almost 30% whether the tuberculin reactions were large or small. This finding is contrasted with that in the southern part of the United States where in an area in which non-specific tuberculin sensitivity is common the prevalence in unvaccinated reactors was 1·2% and was much higher among those with large than those with small reactions. *H. G. Calwell*

JUSTINIANI C., A. Estudio preliminar de 200,000 exámenes de Roentgen-Catastro Torácico. [**Preliminary Study of 200,000 Chest Examinations by Mass Radiography**] *Bol. Epidemiólógico.* México. 1959, Jan.–Feb.–Mar., v. 23, No. 1, 21–7.

The work was done in Monterrey by a mobile Westinghouse machine between September 1952 and May 1958: 35 mm. films were used: the staff comprised the director, a secretary, 2 nurses, a chauffeur and a mechanic: a free examination was offered to the general public and the machine was moved from point to point to suit the convenience of the various groups. The daily number of examinations was between 300 and 500.

Abnormalities found numbered 16,608 (83 per 1,000 examined): of which 5,246 (26·2 per 1,000) were probably pulmonary tuberculosis; 1,859 (9·3 per 1,000) were cardio-vascular lesions and 9,503 (47·5 per 1,000) other abnormalities.

Analysis of the 5,246 with "probably pulmonary tuberculosis" showed 4,561 (22·8 per 1,000) with minimal lesions; 473 (2·4) moderately advanced and 212 (1·0) very advanced.

Two tables give the findings among population groups showing less than average incidence and more than average: the former include the teachers and scholars of schools in certain districts, university students, bank clerks and soldiers: the incidence is high in other schools and, as was expected, among those attending hospitals and clinics.

An analysis by years shows no decline in the ratios with probably pulmonary tuberculosis: in 1952 when few were examined the incidence was 39·9 per 1,000; in 1953, 14·7 rising to 30·8 in 1956 and to 46·5 in 1958. The proportion with serious lesions is, however, falling sharply: for very advanced it fell from 10·7% in 1952 to 1·9% in 1958 and for moderately advanced from 18·2 to 3·6%.

The campaign has been of value in drawing general attention to the importance of health and in discovering hitherto unknown cases of pulmonary tuberculosis in the early and treatable stages.

MACHIAVELLI (*The Prince*, circa 1513) is quoted; the relevant passage in the English version [London, Dent, Everyman's Library 1911, pp. 21–22] is as follows: "as the physicians say it happens in hectic fever, that in the beginning of the malady it is easy to cure but difficult to detect, but in the course of time, not having been either detected nor treated in the beginning, it becomes easy to detect but difficult to cure."

Exact figures are not given of the proportion of the

population who were X-rayed but it is stated that many more could have presented themselves.

The 3 stages in the control of pulmonary tuberculosis are:

(1) sufficient chest X-ray surveys,
(2) adequate chest clinics, and
(3) modern drugs at a low cost. *Allen Daley*

VASQUEZ, G. & LATTIMER, J. K. **Danger to Children of Infection from Exposure to Urine containing Tubercle Bacilli. Results of a Study made with the Mantoux Test.** *J. Amer. Med. Ass.* 1959, Sept. 5, v. 171, No. 1, 29–33, 4 figs.

Patients with genito-urinary tuberculosis are not generally regarded as infectious and the precautions which would be needed if pulmonary tuberculosis were present are rarely taken.

In order to obtain evidence whether in fact the urine of such patients could spread infection the authors carried out tuberculin tests on the children of their patients who had genito-urinary tuberculosis. They selected children exposed to such patients excluding those with concurrent open pulmonary tuberculosis. There were 50 children representing the results of 5 years' testing and case-finding among a group of some 300 men and women with genito-urinary tuberculosis.

The children were exposed to risk during the period when the urine was known to contain tubercle bacilli. Those over 12 years of age were excluded arbitrarily. The Mantoux test was used with 1–100 TU of OT.

50 children were accepted into the trial and tested. They were the progeny of 28 parents. 11 (22%) were reactors and 39 (78%) non-reactors. The reactor rate was significantly higher than the rate of 10% or less which was found in the general population of the same age-group in the surrounding area of the United States. All reactors were examined carefully and in no case was evidence of the primary lesion demonstrated. It was conjectured that the lesion might be in the gastro-intestinal tract, probably owing to the ingestion of tubercle bacilli from the infected urine of the patient.

It is the authors' policy to remove children from the household of a patient with genito-urinary tuberculosis at least until he begins specific chemotherapy. Special precautions should be taken by patients to avoid spreading infection by their urine. A separate laundry bag should be used and contaminated clothing washed separately.

Children at risk should be tuberculin tested up to 100 TU and non-reactors retested approximately every 6 months. [There is no mention of BCG vaccination for these children.] Reactors should be X-rayed and given a thorough clinical examination. Consideration might be given to preventive chemotherapy.

*H. G. Calwell*

LANGEROVÁ, M., ZAVADILOVÁ, Z. & SOUKUPOVÁ, T. Výsledky bakteriologických studií při pitvách zemřelých na tuberkulózu plic a návrh hygienických opatření k ochraně personálu prosektur. [**The Results of Bacteriological Studies on Post Mortem Material from Pulmonary Tuberculosis, and a Suggestion for Hygienic Measures for the Protection of Post Mortem Room Personnel**] *Časopis Lékařů Českých.* Prague. 1959, June 12, v. 98, No. 24, 746–8. English summary.

The authors have investigated the extent of contamination with *Mycobacterium tuberculosis* of a post mortem room during 6 autopsies on persons who had died from pulmonary tuberculosis. In an examination of 185 swabs taken from various objects in the room, cultures of *Myco. tuberculosis* were isolated in 108 instances (60%). Of these positive results 6 (11%) were obtained in 51 examinations carried out before the autopsy had begun, 78 (86%) in 89 during the autopsy, 23 (76%) in 31 during washing down and 1 (0·7%) in 14 examinations made after disinfection of the room had been carried out. *Myco. tuberculosis* was also isolated from the environment in 9 of 79 tests (13%) carried out during autopsies on persons who had died from other causes than tuberculosis. Routine measures for limiting the spread of infection are discussed.

*D. J. Bauer*

HEAF, F. **The Techniques of Tuberculin Testing.** *Acta Tuberculosea Scandinavica.* 1959, Suppl. 47, 153–61, 2 figs. [31 refs.]

It was in 1890 that Koch described the phenomenon that bears his name, and ever since that time work has gone on to find a single tuberculin test that is simple to perform, gives a clear reaction and is specific and selective.

Heaf describes the various tests that are used in current practice.

*The Moro Ointment Test*: An area of skin about 20 cm. square is rubbed with an ointment containing 40% OT. The area is covered with a dry dressing. The criterion of a positive reaction is induration with 3 or more vesicles after a lapse of 72 hours.

*The Jelly Patch Test*: A jelly containing 60% OT is applied to the skin on 2 lines each 6 cm. long (V-shaped). Strapping is applied and removed at 24 hours. The criterion of a positive reaction is as in the Moro test. The skin may be abraded gently with flour paper before the jelly is applied.

*The Trambusti Test*: This is made by placing a small drop of undiluted OT on the skin of the forearm which is pierced intradermally to 5 mm. along the shaft of a number 12 injection needle. The needle is raised to 45° twisted 2 or 3 times and then withdrawn. The reaction is read in 3 days and an induration of 6 mm. in area constitutes a positive result.

*The Von Pirquet Test*: One scratch 5 cm. long is made through the epidermis on the outer surface of the forearm with a sterile lancet or needle or nib. A drop of adrenalized undiluted OT is rubbed into the scratch and the site left uncovered for 5 minutes. The criterion of a positive reaction is induration of 3 mm. or more across the scratch at 72 hours.

*The Mantoux Test*: An intradermal injection of OT or PPD is given and an induration of 5 mm. (or more) at 72 hours is considered to be a positive reaction. The dose of tuberculin varies from 1 to 100 TU. (1 TU

equals 0·01 mgm. of OT or approximately 0·00028 mgm. of PPD.)

*The Multiple Puncture Test (Heaf)*: The special instrument designed by the author is used. He recommends that PPD (2 mgm./ml.) be used. The test is read on the third to seventh day and 4 or more indurated papules or any more severe reaction indicate a positive reaction.

Heaf emphasizes the need for strict attention to detail in all tuberculin testing both in performing the test and in reading and recording the reaction.

The tests described above are discussed. The ointment and jelly tests are simple but they produce too many doubtful reactions. The Trambusti test is simple but indefinite when the reactions are small. The von Pirquet test involves a high personal factor in that so much depends on the depth of scarification. It has also the disadvantage, common to all tests except the Mantoux, that the dose of tuberculin entering the skin is variable and uncertain. The Mantoux test is accurate but requires skill to perform correctly. The Heaf test [which is excellent] has among its other virtues the use of stable tuberculin and the fact that the test can be read up to 7 days after it is done.

Some of the difficulties of tuberculin testing arise from the tuberculin and the response of the tissues rather than from technique. To overcome these, studies are being made on OT, PPD and BCG tuberculin. Further improvement is desirable in view of the increasing importance of the test in epidemiological work. *H. G. Calwell*

EDWARDS, Lydia B., EDWARDS, Phyllis Q. & PALMER, C. E. **Sources of Tuberculin Sensitivity in Human Populations. A Summing up of Recent Epidemiological Research.** *Acta Tuberculosea Scandinavica.* 1959, Suppl. 47, 77–97, 11 figs. [24 refs.]

It is becoming recognized that mycobacteria of different types may cause the tuberculin sensitivity formerly attributed only to the virulent type of tubercle bacillus. The research section of the Tuberculosis Programme of the United States Public Health Service is making a study of the subject, and some of the findings are presented in this paper. The Mantoux test was used with PPD-S, and reactions were measured rather than recorded as positive or negative.

For many years anyone who reacted to any dose of tuberculin was regarded as having had a tuberculous infection but doubt about this began to arise because of the disparity of results obtained from testing tuberculous patients and other groups of the population. Most reports indicated that almost all persons with active tuberculosis reacted to 5 or 10 TU but studies among healthy groups showed that there were large numbers who reacted only to large doses of tuberculin.

Examples of such studies and results in the United States are given showing the geographical distribution of the different patterns of tuberculin sensitivity and presenting evidence that signs of tuberculous infection were closely associated with reaction to 5 but not to 250 TU.

The evidence available pointed to the conclusion that sensitivity to 5 TU is largely the result of tuberculous infection but most of the reactions to the large doses are caused by cross reaction due to infection with another organism or organisms closely related antigenically to the human type of tubercle bacillus and rarely pathogenic for man.

Small reactions to 5 TU appeared to have the same significance as the sensitivity elicited more readily by doses of 100–250 TU, suggesting that some of the small reactions classified as positive to 5 TU as well as most reactions to large doses are cross reactions. Recent studies of different population groups in the United States, of which details are given, support such a view.

As far as tuberculosis control is concerned the urgent practical problem is to differentiate persons with true tuberculous infection from those with non-specific infections, and studies to this end were made. Comparative testing was started with antigens prepared from such acid-fast organisms as avian and bovine tubercle bacilli, *Mycobacterium balnei* and *Myco. phlei* and several others including chromogenic saprophytes, several strains of non-photochromogenic mycobacteria (Battey type) and a variety of others.

Tuberculous patients had, in all but a few cases, larger reactions to PPD-S than to avian or other tuberculins. In one trial comparative tests with PPD-S and PPD-Battey separated patients infected with the Battey organism from patients infected with human type tubercle bacilli.

A reliable method of distinguishing between specific tuberculin reactions and cross reactions depends on the development of appropriate antigens and techniques for comparative testing. *H. G. Calwell*

SOMNER, A. R. **Observer Disagreements in the Interpretation of Hilar Shadows in Chest Radiographs.** *Tubercle.* 1959, Aug., v. 40, No. 4, 245–50.

Several papers have appeared recently which emphasized the high percentage of disagreement in the interpretation of X-ray films by different observers. Shadows occurring in the hilum regions have a particularly high "observer error" rate.

This paper deals with 69 patients with 138 hilar shadows. Clinicians with full knowledge of the clinical and bronchoscopic findings interpreted these as 116 normal, 12 suspicious enlargement, and 10 definitely enlarged abnormal shadows. Of the 12 suspicious hilar shadows no abnormality was found in 5, and carcinoma was found in 7 cases. In the 116 normal hilar shadows, 12 were interpreted as "normal" although a main bronchus carcinoma was known to be present. Where no tumour was found at bronchoscopy, none developed within 2 years.

The 138 hilar shadows were then seen by 4 radiologists, 5 thoracic surgeons, 4 chest physicians, and 5 of their staff, a total of 18 observers. Of the 116 "normal" shadows, 78 were reported as "abnormal" by 1 or more observers. Of the 78 hilar shadows so reported, 26 were reported as abnormal by 1 single observer and 22 by 2.

Details are given of the different variations. The

extent of the disagreements seems to be due to the fact that 2 or 3 of the observers consistently had a bias in favour of diagnosing as suspicious, hilar shadows which the clinicians with the full facts at their disposal classified as normal.

There was no evidence that any particular observer differed appreciably from the rest in ability to discriminate between normal or definitely abnormal hilar shadows. *F. H. Young*

AMERICAN TRUDEAU SOC. **The Chest Roentgenogram and Chest Roentgenographic Surveys related to X-Ray Radiation Effects and Protection from Radiation Exposure. A Statement of the Committee on Radiation Effects** [STOCKLEN, J. B. Chairman]. *Amer. Rev. Respiratory Dis.* 1959, July, v. 80, No. 1, Pt. 1, 115–17.

This is a revision of the earlier statement of the American Trudeau Society issued in 1957. Recently some disquiet has become apparent about the effects of diagnostic radiology. When people are ill X-ray studies are necessary; the definite benefits overshadow the possible hazards of radiation, but X-ray machines vary in the amount of radiation they produce. It is thought that, in children and many others, tuberculin tests can often obviate the use of X-rays. The radiation produced by taking a standard 17 × 14 inch film on a well protected unit is 5–20 times less than that produced by a photofluorographic machine. The mirror optical type of machine is much the safest. Screening by fluoroscopy produces a considerable amount of radiation, both of the patient and the examiner, as does tomography.

The effects of small doses of radiation are at present uncertain. The following techniques are recommended to cut down radiation: proper coning; proper filtration; adequate shielding; adequate tube housing; high kilovoltage; 5–6 ft. skin-to-tube distance; where there is multiple and frequent exposure radiation monitoring should be carried out annually. If this is done the effects do not justify the withholding of necessary X-ray examinations. *F. H. Young*

HILL, Lisa E. & PEARSON, J. E. G. **Bronchial Abnormalities after Primary Tuberculosis.** *Brit. J. Dis. Chest.* 1959, July, v. 53, No. 3, 278–95, 3 figs. on pl. [45 refs.]

There is a considerable divergence of opinion about the residual effects of primary pulmonary tuberculosis with segmental collapse. After a short discussion on the literature (a table is given), 2 investigations are reported.

In the first, 116 children admitted to Frenchay Hospital, Bristol, were considered suitable for bronchography, though for various reasons bronchography was only carried out in 78, of whom 7 were excluded from the study, leaving 71. Of these, 29 (40·8%) had frank bronchiectasis, 3 had a definite and 1 a probable stricture, 10 patients (14%) had irregularity of the bronchi short of bronchiectasis, 5 (7%) had crowding of the bronchi; in 2 the segment affected failed to fill, suggesting a bronchial stricture. 24 (33·8%) were completely normal. Bronchial abnormalities were commoner in lower age-groups. 25 children were bronchoscoped, 21 of whom had some bronchial abnormality. Of the 47 children with bronchial abnormalities, 14 (29·7%) developed lesional symptoms when under observation.

In the second part of the investigation a retrospective study of the records of all bronchiectatic patients admitted during a 10-year period was carried out. Of 562 patients, 30 (5·9%) were thought to have developed bronchiectasis after tuberculosis. All had bronchiectasis of the cylindrical type.

The younger the child and the longer the period of the collapse the higher was the percentage of bronchiectasis.

The authors quote with approval WILLIAMS and ANDERSON (*Quart. J. Med.*, 1953, v. 22, 295) who state that the standard antituberculous drugs have little effect on the primary complex or likelihood of collapse. The authors are cautious on the subject of bronchoscopic removal of tissue in the bronchus, which may be dangerous and ineffectual, and on thoracotomy on a large scale which is probably unavailing.

The authors think that caseation without an obstruction does not produce bronchiectasis. A number of details are given in the text. *F. H. Young*

MCCARTHY, T. F. & MISRA, D. P. **Bronchography in Pulmonary Tuberculosis.** *Brit. J. Dis. Chest.* 1959, July, v. 53, No. 3, 319–23.

The paper reports the results of bronchography on 114 patients, mainly between 20 and 50 years of age, whose tuberculosis had become quiescent. The bronchiectasis when found followed the distribution of the tuberculosis.

Where the radiological findings were nil or minimal (92 lungs) only 1 case, and that mild, of bronchiectasis was found; 13 lungs with severe disease all had severe bronchiectasis. In 19 resection specimens bronchial dilatation was found, bronchiectasis having been previously demonstrated by bronchography. A discussion on conventional lines follows. *F. H. Young*

LÖFGREN, S. & CALLANS, Alice. **Asian Influenza and Pulmonary Tuberculosis.** *Acta Med. Scandinavica.* 1959, Aug. 31, v. 164, No. 6, 523–7. [21 refs.]

This paper commences with a short but interesting account of the effect on tuberculosis of the great epidemic of Type A influenza in 1918–1919. The abrupt halt in the fall in the death rate in Sweden where war privation was not prevalent, followed by a dramatic fall in the 2 succeeding years, indicated its disastrous effect on tuberculous patients; and GULLBRING (*Hygiea*, 1919, v. 81, 593), showed that it was the influenzal pneumonia rather than the uncomplicated influenza which produced this result. The authors determined to assess the effect of the 1957 (Asian) influenza epidemic on tuberculosis. They report on all the 204 patients admitted to the Department of Pulmonary Diseases of St. Göran's Hospital, Sweden from 1st October 1957 to 31st March 1958. 24 of the 158 patients admitted for progression of known pulmonary tuberculosis had a

definite history of influenza, and 4 of the 46 newly detected cases also had a similar history; a total of 13·7%. In 14 other patients the definite proof of influenza was incomplete but highly probable, making a probable total of 20·6%. The deterioration in patients following the influenza was commonly discovered 2 to 6 weeks after the attack. The authors conclude that particular attention must be paid to this possibility in the follow-up studies of patients suffering from pulmonary tuberculosis.

[This paper is worth reading.] *F. H. Young*

TAUTE, J. F. & RABIE, C. J. **Domiciliary Treatment of Pulmonary Tuberculosis in a Rural Area. A Preliminary Report on 7,858 Cases treated in the Transkeian Territories.** *Brit. J. Dis. Chest.* 1959, Oct., v. 53, No. 4, 372–84.

The Transkei is an area in Cape Province, South Africa. It has a population of 1·6 million Bantu and 18,000 Europeans. The Bantu live in isolated huts and the Europeans in villages of 150–600 inhabitants. The extent of the area is over 16,000 sq. miles and much of it cannot be traversed during the rainy seasons. It is estimated that 240,000 Bantu males are continually away working in the mines or other industrial areas. The main crop is maize and cattle are kept as property rather than food.

Domiciliary treatment of tuberculosis was begun in 1955, when the number of persons with active pulmonary disease was estimated as 25,000–30,000. Only 500 hospital beds were available for these patients. There were some 300 treatment centres and 12 X-ray units. The diagnosis was confirmed radiologically in about 75% of cases.

From 1957 onwards the standard treatment was 2 gm. of streptomycin weekly and 10–12 mgm./kgm. of isoniazid daily. 80% of the patients live within 5 miles of a treatment centre.

After 2 years of the scheme information about its working and results was sought. The total number of cases diagnosed was 16,000 but the enquiry was limited to areas where the original skiagrams were available. The total number of patients included in the survey was 7,858.

In the age-group 0–5 years about 40% had more than a primary complex. At 16–34 years females predominated being 62% of the total; this group had the highest proportion of grossly destructive lesions. More females than males were thus affected. In persons aged 35 years and over (53% of the total cases) advanced lesions were found in 51%.

The disease was of recent origin in 52·5% and predominantly fibrotic in 47·5%. Of 3,991 patients entering the scheme 1,636 had resided in urban areas for periods over 2 months and 1,105 of them had worked underground in gold mines.

There is a tendency towards earlier diagnosis which can be considered favourable only if the number of cases diagnosed is falling.

The overall defaulter rate did not appear to be affected by the type of disease. It was 20% in the first 6 months' term and 14% in later terms. 50% fail to complete the prescribed period of 2 years. The fate of defaulters has not yet been examined but it is hoped to do so shortly. There was no difference in the rate of default among those who had had a spell in hospital and those treated only at home.

There was evidence that those who improve or become worse cease to attend; the best attenders were those whose skiagrams showed no change in the first 6 months.

The results of treatment were good in patients whose disease was of recent origin and poor in those with fibrotic lesions. Whether a patient had 1 or 5 injections of streptomycin per month did not appear to matter but the patient who took the isoniazid regularly was expected to do well. Satisfactory improvement was seen in 15·8, 23·5 and 27·0% of the total at 6, 12 and 18 months respectively.

1 specimen of sputum only was collected from patients at the time of diagnosis and follow-up and only direct examination was possible. At the commencement of treatment the sputum was positive in 33% of 659 patients, after 6 months' treatment it was positive in 20·5% of 1,194 patients and after 1 year in 28·2% of 1,483 patients.

"On the strength of available information it is not possible to predict the effect of the present approach on the tuberculosis problem in the Transkeian Territories." *H. G. Calwell*

BULL. WORLD HEALTH ORGANIZATION. Geneva. 1959, v. 21, No. 1, 51–144, 2 text figs. & 10 figs. on 10 pls. [Numerous refs.] **A Concurrent Comparison of Home and Sanatorium Treatment of Pulmonary Tuberculosis in South India** [TUBERCULOSIS CHEMOTHERAPY CENTRE, Madras].

It is estimated that in India there are 2·5 million patients suffering from active tuberculosis, of whom at least 1·5 million are infectious. To deal with these by sanatorium treatment is impracticable in the foreseeable future. On the other hand it was felt that to plunge blindly into a programme of home care without any real knowledge of the likely results of treatment and of the danger of producing vast numbers of resistant organisms was very rash. Accordingly a controlled trial of the 2 methods under conditions existing in India was undertaken with the help of the World Health Organization.

The trial was designed to answer a number of questions but the report deals with 2:—

1. The relative merits of home and sanatorium treatment with standard chemotherapy.

2. The extent to which the infectivity of a series of patients treated at home can be reduced by standard chemotherapy. The remainder will be dealt with in a subsequent report.

The patients were drawn from the poorest section of the population of Madras City and criteria of selection and the pre-treatment investigations were laid down carefully.

The standard medication was a dose of 8 cachets, given 4 in the morning and 4 in the evening, and totalling 200 mgm. isoniazid and 10 gm. of PAS daily, with a reduced dose for patients of lower weights.

The lower average weight of patients meant that this represented a higher dosage than would be the case if it were given to average English patients.

The main analysis deals with 82 patients treated at sanatorium and 81 matched patients who were treated at home. The investigation followed the procedure of the British Medical Research Council trial [this *Bulletin*, 1955, v. 30, 406] very closely, and covers 12 months from September 1956.

Of the male patients (99) 2 of the home-treated patients and 1 of the sanatorium patients died. At the end of 12 months, sanatorium patients had a larger weight gain and a statistically significant reduction in erythrocyte sedimentation rate, and a slight advantage in radiological improvement. 9 of the home-treated and 10% of sanatorium patients still had a positive sputum culture; 9% of the home and 4% of the sanatorium patients still had bacilli resistant to isoniazid.

In the 64 females, 1 sanatorium patient died after 5 days' treatment. The weight gain and sedimentation improvement paralleled the male results; 24% of the home and 3% (and 1 death) of the sanatorium patients had positive sputa. 8 (24%) of the home-treated, and 1 (3%) of the sanatorium patients had active disease. [By chance the home-treated patients had more severe disease than the sanatorium group, and subsequent review suggests that this largely determined the difference in results.]

The self administration of the cachets was supervised both by tests on the urine and by counts of the stock of cachets, and this revealed a difficulty in obtaining the long term cooperation of patients treated at home in taking their medicine. More irregularity in self administration was found among female than among male patients.

The majority of the home patients were living in over-crowded conditions, the families of 68% of the males and 85% of the females having less than 45 sq.ft. (4·2 m.$^2$) of living accommodation per person; 20% of the families of the males and 48% of the females had less than 25 sq.ft. (2·3 m.$^2$) per person. 2 males (4% of the 47 studied) were homeless.

Whereas major social problems arose in 20 of the families of the 97 patients in sanatorium they occurred in only 8 of the 96 home families, and were also less serious; thus, in this study, sanatorium treatment proved more disruptive to family life.

12 of the 97 sanatorium patients were discharged during the 12 months (though 4 were only temporary discharges) whereas only 1 of the 96 home patients discharged himself from treatment. It proved easier to keep the co-operation of the home patients.

*F. H. Young*

COHN, M. L.; MIDDLEBROOK, G.; RUSSELL, W. F., Jr.; MANDEL, W.; HEATON, Angeline D.; KASS, I.; DRESSLER, S. H.; DENST, J. **Combined Drug Treatment of Tuberculosis. I. Prevention of Emergence of Mutant Populations of Tubercle Bacilli Resistant to both Streptomycin and Isoniazid** *in vitro* [COHN, MIDDLEBROOK & RUSSELL]. *J. Clin. Investigation.* 1959, Aug., v. 38, No 8, 1349–55. [21 refs.] **II. Studies of Antimicrobially-Active Isoniazid and Streptomycin Serum Levels in Adult Tuberculous Patients** [MANDEL, HEATON, RUSSELL & MIDDLEBROOK]. *Ibid.*, 1356–65, 3 figs. [34 refs.] **III. Clinical Application of the Principles of Appropriate and Adequate Chemotherapy to the Treatment of Pulmonary Tuberculosis** [RUSSELL, KASS, HEATON, DRESSLER & MIDDLEBROOK]. *Ibid*, 1366–75. [32 refs.] **IV. Bacteriologic Studies on the Sputum and Resected Pulmonary Lesions of Tuberculous Patients** [HEATON, RUSSELL, DENST & MIDDLEBROOK]. *Ibid.*, 1376–83. [21 refs.]

I. The authors note that experiments purporting to prove the undoubted clinical superiority of multiple drug therapy against *Mycobacterium tuberculosis* are inadequate because the number of organisms tested have been few and liquid media have been used. They consider that it is necessary to deal with the prevalence of mutants resistant to 2 drugs in wild, previously unexposed populations of tubercle bacilli. The method adopted is described. Pearson I strain of bacilli and H37Rv were used. A series of experiments gave the following results.

Concentrations of streptomycin not quite sufficient alone to inhibit the growth of all streptomycin-susceptible bacterial cells were remarkably effective in combination with 20 times the minimum inhibitory concentration of isoniazid in reducing the emergence of drug-resistant mutants. Concentrations of isoniazid, whether only slightly or far in excess of the minimum inhibitory concentration, when combined with the minimum sterilizing concentration of streptomycin prevented the emergence of any drug-resistant mutants. Prevention of emergence of drug-resistant mutants was attributed to the cross-sterilizing action of the two drugs on individual mutants separately resistant to each one. The implications of these observations for clinical chemotherapy were discussed.

II. It is gradually becoming clear that the use of standard daily doses of streptomycin 1 gm. and isoniazid 4–5 mgm. per kgm. is by no means adequate to deal with tubercle bacilli in many patients. Many factors determine the concentrations of these agents to which multiplying tubercle bacilli are exposed in the human subject: dosage; absorption and excretion; metabolic alteration; binding to protein; and diffusion into lesions, tissues and cells. Furthermore, with streptomycin the problem is complicated by the presence of substances in the lesions which antagonize the antibacterial action of the drug. Isoniazid is altered to derivatives such as acetyl-isoniazid and isonicotinic acid which have little or no antimicrobial activity. Many observers have found that the rate of metabolic alteration of the isoniazid molecule varies widely in different people, and this produces a varying result in the bacteriological response in treated patients [this *Bulletin*, 1957, v. 32, 615].

This study deals with specific microbiological assays on sera from treated patients. Sera from 254 patients were examined. The trial of various drugs on the antimicrobially active serum showed that PAS and PABA had usually a large adjuvant effect, other drugs had none.

A figure is given showing the great variation of serum isoniazid levels in 254 patients. In 5 patients tested the isoniazid level was the same in cavities and serum. Approximately 45% of the 254 patients failed to achieve a level of 0·8 μgm. at 6 hours after a dose of isoniazid 4 mgm. per kgm.

The results of application of a microbiological assay method for serum streptomycin are also presented, and, as previously shown for isoniazid, a significant relationship is demonstrated between serum levels of streptomycin and certain aspects of the microbiological response in patients to streptomycin treatment.

The clinical implications of the variations in antimicrobially-active serum levels of both isoniazid and streptomycin achieved by different patients are discussed.

III. The variation of drug serum levels suggest that conventional dosages could not be relied upon to ensure the delivery *in vivo* of sterilizing concentrations of each agent to physiologically-susceptible tubercle bacilli. The result of consideration of these principles was the formulation of a chemotherapeutic regimen combining high dosage of streptomycin with high dosage of isoniazid for all patients. The purpose of this report is to present the results of clinical application of this approach to chemotherapy of pulmonary tuberculosis.

The paper deals with 318 patients divided into 3 categories. Group I patients were excreting streptomycin-susceptible, isoniazid-susceptible populations of tubercle bacilli. Group II patients were excreting either streptomycin-resistant, isoniazid-susceptible or streptomycin-susceptible, isoniazid-resistant populations. Group III patients were excreting streptomycin- and isoniazid-resistant populations. All patients of Groups II and III (except possibly 1) who were excreting isoniazid-resistant populations of tubercle bacilli gave histories of at least 3 weeks' previous treatment with isoniazid or its chemical derivatives. Similarly, all, except 4 patients, who were excreting streptomycin-resistant populations gave histories of previous streptomycin or dihydrostreptomycin treatment.

A basic therapeutic regime consisted of streptomycin sulphate (Squibb) 1 to 2 gm. daily (20 mgm. per kgm. per day or more in those patients who had low streptomycin serum levels), by the intramuscular route in a single dose, for at least 90 days. Streptomycin was not discontinued until the sputum was negative on smear and culture of the concentrate. Isoniazid (Nydrazid, Squibb) 16 or more mgm. per kgm. per day, was administered orally for at least 18 months. Isoniazid was given in 2 equal doses each day. Pyridoxine hydrochloride (Squibb), 50 to 100 mgm. per day, was also given orally for 18 months. Pyridoxine was included in this regimen to reduce the incidence of significant isoniazid neuropathy [this *Bulletin*, 1956, v. 31, 1211]. It should be emphasized that after termination of streptomycin, the isoniazid and pyridoxine were continued alone.

Patients in Group II had in addition NaPAS 12 gm. daily. Those in Group III were treated with a variety of combinations of drugs but all included isoniazid.

152 of Group I patients had sputum conversion within 6 months, but 1 relapsed with resistant organisms. In the 51 patients with demonstrable cavities, all these were closed in 5–8 months; 66 patients had persistent cavities (open cavity healing). Group II patients (40) at the same time had only 19 conversions. Group III patients converted in only 33 out of 125. In other patients treated by streptomycin twice a week the results were much less good. Significant drug reactions occurred in 12% of the patients.

IV. This section deals with the relationship between pre-operative sputum examinations and results and the bacteriology of the specimens removed by resection. It covers 220 patients, divided into groups. Some of these were original treatment cases, of whom 24 were treated by conventional antimicrobial doses and 49 by the high dosage system, *i.e.* 20 mgm. per kgm. streptomycin per day with 16 mgm. or more isoniazid per kgm. per day, together with pyridoxine 50 to 100 mgm. daily; PAS was added when indicated. The remainder were patients who had had long periods of antimicrobial treatment unsuccessfully before admission. At the time of resection 107 patients were not sputum converted, 11 belonging to the 73 original treatment patients, and 96 to the 147 retreatment patients: the remaining 113 were sputum negative. Of the lesions studied, 144 (48%) were positive on culture, three-quarters of these being cavitated lesions. Of the remaining 154 culture-negative lesions one-half were positive on smear. The number of solid lesions culture-negative was twice as great as the number of cavitated lesions.

In 206 of the total 220 patients there was complete agreement in the bacteriological results of the study of the pre-operative sputum specimens and of the resected specimens. Anomalous results were obtained in 14; these are discussed in detail. Of the 139 lesions from the 113 converted cases, all but 3 of the 46 open cavities were negative on culture, and three-quarters were negative on smear. Of the 10 filled cavities, none were negative both on smear and culture. Of the 159 lesions from the 107 patients with positive sputum, 104 of the open cavities were positive on culture. 10 of the 18 filled cavities were positive on culture. 75% of the 28 nodular lesions were positive on culture. Identical pattern drug-susceptibility of the tubercle bacilli recovered from sputum and resected lesions was found in 94 patients. These and other results are fully discussed.

The high incidence of bacteriologically negative results on resected specimens from sputum-negative patients treated by the high dosage system indicates its efficiency.

[These 4 papers emanate from the pathological laboratories of the National Jewish Hospital at Denver, Colorado, whose standard of work is generally accepted as unsurpassed by any other in the world. The papers are of highest quality and will amply repay the time taken to assimilate the vast quantity of work presented in them; no abstract can deal with it adequately.]

*F. H. Young*

CHAVES, A. D. **A Simple Paper Strip Urine Test for Para-Aminosalicylic Acid.** *Amer. Rev. Respiratory Dis.* 1959, Oct., v. 80, No. 4, Pt. 1, 585–6.

MARMION, T. **The Acceptability of Potassium Para-Aminosalicylate.** *Brit. J. Dis. Chest.* 1959, Oct., v. 53, No. 4, 409–11.

Some patients are unable to tolerate the ordinary therapeutic doses of PAS because of gastro-intestinal disturbances. This report is concerned with tolerance of potassium PAS, the clinical and bacteriological effects of which are similar to those of the sodium salt.

During the previous year Marmion treated 30 patients with potassium PAS as part of their combined drug treatment for pulmonary or renal tuberculosis.

When it was realized that the potassium salt was very well tolerated by patients who had experienced severe symptoms when treated with other forms of PAS the full dose of 12 gm. daily was given.

20 of the patients had uncomplicated pulmonary or renal tuberculosis and all had been unable to tolerate other forms of PAS. No gastro-intestinal upsets were reported following the change to potassium PAS.

Of the remaining 10 patients 3 were mentally unfit for medication of any kind but the drug succeeded in 1 case. One other patient could not tolerate it; he was one of 3 with associated intestinal tuberculosis. The other 2 tolerated the drug, one with little change in the diarrhoea which was probably unconnected with PAS. The remaining 4 patients had symptoms referable to peptic ulceration or to post-operative gastrectomy states, and they tolerated potassium PAS easily.

It was concluded that potassium PAS is of value in the treatment of tuberculosis in patients who cannot tolerate other forms of PAS or in patients for whom a restricted sodium intake is advisable such as those on corticosteroid therapy or suffering from circulatory insufficiency. *H. G. Calwell*

WINBLAD, S., JEPPSSON, Eva & SELANDER, E. **The Development of Mycobacterial Resistance to PAS in Pulmonary Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, No. 3, 187–94. [16 refs.]

These sensitivity tests were made on 230 strains of tubercle bacilli from patients who had been treated with the sodium salt of PAS; the usual dose was 14 gm. a day for adults and it was given with other anti-tuberculous drugs. The sensitivity tests were done on Löwenstein-Jensen medium, in which the PAS had been allowed to diffuse into the medium.

The results show that the incidence of resistant strains increases with the duration or the total dose of drug administered. None of the patients had resistant strains after receiving a total dose of 500 gm., but after receiving a total dose of 5,000 gm., 5,000–10,000 gm. and 15,000 gm. the incidence of resistant strains increased to 15%, 62% and 80%, respectively.

In addition to these strains, 196 were isolated from patients before treatment with PAS and 4·6% were moderately resistant and 2·5% were highly resistant to the drug. *S. R. M. Bushby*

MONEY, G. L. **Isoniazid Neuropathies in Malnourished Tuberculous Patients.** *J. Trop. Med. & Hyg.* 1959, Aug., v. 62, No. 8, 198–202, 1 graph. [14 refs.]

During the course of a chemotherapeutic bacterial sensitivity trial in Ibadan, Western Nigeria, 84 patients (49 male and 35 female) undergoing ambulatory treatment for pulmonary tuberculosis were examined for evidence of neuropathy. It was presumed that all were suffering from some degree of malnutrition.

The treatment consisted of 300 mgm. (4·6 mgm./kgm.) of isoniazid and 12 gm. of PAS by mouth daily. No vitamin or other food supplements were given. At the time of the survey 15 patients had been treated for 6 months, 48 for more than 6 and less than 10 months, and 21 for 10–12 months. Evidence from a previous trial in the same place had indicated that nervous complications rarely developed before the end of 6 months' treatment with isoniazid.

16 patients, 9 men and 7 women, were found to have neurological disease (about 20%). There was predominantly sensory polyneuropathy in 13 and vasculo-neuropathy in 3. 1 patient with polyneuropathy had bilateral retrobulbar neuropathy.

The distribution of these cases according to the time of onset after the start of treatment was analysed: 6 months, 1 case; 7 months, 1 case; 8 months, 6 cases; 9 months, 3 cases; 10 months, 2 cases and 11 months, 3 cases. These figures suggest that isoniazid neurotoxicity is cumulative and not a hypersensitivity reaction.

The clinical types of isoniazid neuropathy seen were studied both in the survey group and in other patients admitted to hospital with pulmonary tuberculosis and receiving isoniazid. Excluding "intangible neurasthenic" symptoms the important groups were:

3 patients showing the painful feet syndrome (4–5%); the chief symptoms were pains and burning sensations in the soles of the feet with hyperaesthesia and excessive sweating. These patients were treated with 12 tablets of yeast daily, isoniazid being continued. After 1 month they were much relieved. This syndrome is related to pantothenate deficiency [*Trop. Dis. Bull.*, 1946, v. 43, 768].

13 patients with polyneuropathy (15–16%); it was usually symmetrical and affected the legs more than the arms. Sensory functions were more affected than motor functions. This was the commonest organic neurological manifestation of isoniazid toxicity. Most patients were able to continue the course of isoniazid with addition of vitamin B.

Other symptoms encountered were blurring of vision with acute retrobulbar neuropathy (1), backache and girdle sensation (2), impotence (1).

3 patients were seen (not in the survey group) who developed spastic paraplegia which responded to the withdrawal of isoniazid and the administration of vitamin B by injection.

Acute psychoses were seen in 8 patients in hospital all of whom were very ill with tuberculosis and malnutrition. The mental disturbances occurred within a few days or weeks of starting treatment with isoniazid. Withholding the drug and giving vitamin B complex resulted in remission.

These results support the view that deficiency of vitamin B increases the incidence of isoniazid neurotoxicity particularly in the presence of PAS. Since isoniazid is being increasingly used in tropical countries

caution must be exercised particularly where there is reason to suspect vitamin B deficiency. Pyridoxine is expensive and will not correct multiple deficiencies. Yeast should be used routinely.

[See also *Trop. Dis. Bull.*, 1958, v. 55, 933: 1959, v. 56, 868.] *H. G. Calwell*

LAZAROU, P. Manifestations neurotoxiques chez un tuberculeux au cours du traitement à grandes doses d'isoniazide (I.N.H.). [**Neurotoxic Signs in a Tuberculous Patient treated with Large Doses of Isoniazid**] *Acta Tuberculosea Scandinavica.* 1959, v. 37, Nos. 1/2, 137–50. [Numerous refs.]

This paper describes and discusses a patient who was in error given very excessive doses of isoniazid. This amounted to 30 tablets of 0·2 gm. Neoteben in 110 hours; *i.e.*, 6 gm. in 4½ days. The study of the patient was complicated by the simultaneous use of streptomycin and PAS given in normal doses; *i.e.*, 3·25 gm. of streptomycin and 47 gm. of PAS in 5 days. He had been treated previously with streptomycin and after receiving 10 gm. had suffered intense vertigo. On the occasion described he received 9 tablets in 12 hours and complained of headache and slight vertigo. On the 5th day the patient complained of palpitations, extra systoles and intense vertigo, giddiness, and noises in the ears. Later in the day he went into semi-coma, became aphasic and had twitchings of the lower limbs and became delirious. On the 6th day he was giddy, had diplopia and went into a profound sleep for 7 hours. He could not stand, and tended to be incontinent of urine. A similar condition persisted on the next day. A neurological examination showed no gross abnormality. A lumbar puncture was performed and a clear fluid was obtained under slight pressure; 10 cc. were removed which was practically normal. Within a short time the patient recovered, all symptoms disappeared and did not recur. The patient was discharged after a further week. The author considers that the symptom picture was caused by cerebral oedema.

The description of this case is followed by a review of the literature on isoniazid toxicity and a full bibliography. *F. H. Young*

See also p. 110, GHISLANDI, [**The Chemotherapy of Silicotuberculosis: Experiences with Pyrazinamide and Cycloserine**].

SHUBIN, H., LAMBERT, R. E., HEIKEN, C. A., SOKMENSUER, A. & GLASKIN, A. **Steroid Therapy and Tuberculosis.** *J. Amer. Med. Ass.* 1959, Aug. 15, v. 170, No. 16, 1885–90, 6 figs. [14 refs.]

In many advanced cases of pulmonary tuberculosis the authors found that a low 17-ketosteroid level existed, and therefore replacement was indicated. The preliminary findings are impressive.

The effect of steroid therapy was investigated in 36 patients with acute, and 107 patients with chronic forms of tuberculosis. The steroid used, prednisolone, was added to the regular regimen of streptomycin, isoniazid, and PAS. It was started at 50 mgm. in divided doses for the first day and gradually reduced to 15 mgm. by the 23rd day. 2 case histories illustrate the recoveries seen in patients with acute tuberculosis; there frequently was rapid objective improvement, and 32 patients recovered, including 8 with tuberculous meningitis. 2 further case histories illustrate the striking results in chronic tuberculosis. The group of 107 included 20 patients who had been expected to die, and 15 of these recovered.

The advantage obtained by the use of steroids in the chronic cases was considerable. A fatal case is reported showing the danger of stopping the steroid therapy before operation. During one year the authors saw 58 patients in whom tuberculosis developed during treatment with steroids for other conditions. Warnings are given that before their use full investigation to exclude latent tuberculosis should be made and antimicrobial drugs used if there is any doubt. [The paper is very interesting but in the absence of matched control cases the results can only be accepted as clinical impressions.] *F. H. Young*

EADE, A. W. T., HARRISON, G. K., LARGE, S. E., MACKAY-DICK, J., REID, Lynne & RIDDELL, R. W. **The Radiological and Bacteriological Assessment of Tuberculous Lung Lesions remaining after Chemotherapy.** *Thorax.* 1959, June, v 14, No. 2, 104–12. [29 refs.]

This assessment was made on 59 Gurkha soldiers who had been treated continuously for 10–25 months with 1 gm. streptomycin and 200 mgm. isoniazid on alternate days (for the first 30–60 days the drugs were given daily). Radiological assessment, which included tomography, of the course of the infection was made at 6-week intervals, and as each of the patients showed more than minimal residual diseases, resection was performed because of the difficulty of continuous follow-up after their discharge. 39 patients had cavities.

Of the 46 cavities observed in these 39 patients at the beginning of treatment, 41 closed during treatment; 5 cavities were still present at the time of operation. 20 of these 39 patients had positive sputum immediately before the resection, compared with only 1 of 20 without cavitation. Positive smears were obtained from the resected specimens of 50 of the patients, and positive cultures from 6 after treatment for 9–25 months. 2 of the strains of bacilli were drug-resistant, and these were from patients who had been treated for 17 and 23 months, respectively.

Of the specimens from the 5 patients with cavitation at the time of resection, 3 yielded viable bacilli. [Brief details of these patients are given.] Tubercle bacilli were grown from only 1 of the specimens from the 34 patients whose cavities had closed during chemotherapy, and this exception was from a patient who had been treated for only 6 months after the closure of the cavity. In the resected specimens from these 34 patients a filled-in cavity was found in 15, a nodule of caseous material in 12, only a thickened pleura in 2, and in 5 no lesions representative of the cavity were

found. In 4 patients, cavities were diagnosed radiologically, but the residue of only 1 was found in the resection specimens. Positive cultures were obtained from 2 of 20 patients with solid lesions, in spite of these patients having had consistently negative sputa.

The authors consider that, in general, these findings support the view that the persistence of viable tubercle bacilli is reduced with increased duration of chemotherapy unless resistance develops. They discuss the significance of these results at some length and conclude that the results constitute a strong argument in favour of resection for patients with persistent cavitation, that prolonged chemotherapy without resection appears to be the treatment of choice for patients with closed cavitation, and that although the value of surgery may be questionable for patients with non-cavitation the finding of viable bacilli after 16 months' chemotherapy undoubtedly suggests that it merits serious consideration. *S. R. M. Bushby*

KREIS, B. **Effectiveness of Antituberculous Treatments tested by Direct Culture of the Bacilli in the Patient's Blood.** *Amer. Rev. Respiratory Dis.* 1959, July, v. 80, No. 1, Pt. 1, 85–8.

The present methods in ascertaining whether a given drug or combination of drugs are efficient in dealing with the tubercle bacilli harboured by any individual patient has certain disadvantages from the clinician's point of view and is time-consuming.

The author describes a method by which tubercle bacilli from sputum are cultured in specimens of blood from the patients under drug treatment. If the concentration of the drugs in the blood is adequate the bacilli will not grow; if there is an insufficient concentration or the patient is not on drugs, or the bacilli are resistant the bacilli will grow freely.

Tables are given showing that the results by this method follow closely those obtained by orthodox laboratory methods.

The disadvantages of orthodox methods of estimation are discussed. This method is especially useful where partial resistance is known to be present. Where bacilli multiply in the blood the treatment is unsatisfactory, but the reverse is not necessarily correct as an adequate concentration of drug may occur in the blood but not in caseous areas.

A study on cycloserine follows. Some 41 patients being treated with cycloserine had their blood tested; in 10 growth occurred, showing that the amount in the blood was insufficient; in the other 31 no growth occurred. Where bacilli from sputum are not available a standard culture is used.

This paper suggests a new approach to the problems arising in drug dosage and drug resistance in individual patients. *F. H. Young*

ALONEN, I. & MÄKIPAJA, J. N. **A Study of Pneumothorax Therapy and its Long-Term Results.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, No. 3, 175–86. [13 refs.]

Artificial pneumothorax has decreased in popularity to such an extent that it is interesting to see a paper on its results and advocating its continuance. Although in the series antimicrobial treatment was used in a number of cases, it would appear from the fact that the paper refers to cases in which pneumothorax was induced in 1947–1949 that it was not used frequently or was used for too short a period pre-operatively. This makes these results from the Central Sanatorium of Middle Finland historical rather than practical in application. Adequate pre-operative drug treatment has reduced the incidence of complications to very small proportions.

The paper deals with the long term result in 381 patients, of whom 20 had bilateral pneumothoraces. 68·5% are now capable of work. 10·5% have died from tuberculosis; of these 90% were exudative cases. On the other hand when the 53·4% of patients who had complications are analysed there is little difference between those who had exudative and those who had productive disease. Complications were 8% higher in incomplete pneumothoraces than when it was complete. Short term pneumothoraces (1 year or less) had much inferior results. At the time of assessment only 40% were inactive. A high erythrocyte sedimentation rate (44 mm./1 hour or higher) prognosed a relatively poor outlook. Only 54% were inactive and 20·6% had died.

Empyema was present in 3% of pneumothoraces. Comparison is made with reports on several series of cases from the United States and Great Britain, and so it is rather surprising that no reference is made to the Frimley series (*Brompton Hospital Reports*, 1952, v. 21, 1).

Neither bronchoscopy, tomograms nor lateral films were generally available, so the correct selection of cases suitable for pneumothorax was handicapped. The authors agree with the general opinion that the duration of the pneumothorax has little effect on the final lung function. *F. H. Young*

GEBAUER, P. W. & MASON, C. B. **Analysis and Late Results of Resection for Pulmonary Tuberculosis in Hawaii.** *Amer. Rev. Respiratory Dis.* 1959, July, v. 80, No. 1, Pt. 1, 6–11.

The paper reports the results of resection in Hawaii on 354 patients between 1946 and 1957 who were followed up for 2–12 years. 84% were originally positive but only 72% were positive at the time of the operation. Only 6 have been lost sight of. 8 patients had no pre-operative antimicrobial treatment, and 16 had grossly inadequate antimicrobial cover.

A table giving the type of operation and result is given. 317 (89%) are well and able to work. There were 8 operative deaths, all with lobectomies and pneumonectomies. 27 had non-tuberculous, 23 had early tuberculous, and 43 late tuberculous complications. There were 2 late tuberculous and 13 non-tuberculous deaths. The complications and causes of death are tabulated. The causes of further disabilities from tuberculosis are then considered, the patients dying at operation and those who had grossly inadequate pre-operative treatment (24) were excluded. Only 8% of patients who had adequate pre-operative treatment had complications. The less adequate the pre-operative

treatment the higher was the complication rate. 60% of those without complications but 22% with complications had chemotherapy for from 4–12 months.

60% of the resected specimens were examined bacteriologically. The resected specimens were negative on culture in 73% of those without complications and in only 33% of those with complications.

The percentage of complications did not vary much between those whose specimens did or did not grow tubercle bacilli. "Less than 1% of the 'uncomplicated' group and 21% of the 'complicated' group had contralateral tuberculous disease recently considered to be cavitary." Involvement of larynx and bronchi increased the complication rate. It is concluded that inadequate pre- and post-operative treatment produced 30% of the complications. Surgical excision was completely successful when adequate pre-operative treatment (6–8 months) had been given, when the contralateral side was normal, when sputum conversion had been achieved, if the original bacilli were drug sensitive and cultures from the resected specimens were negative, and if post-operative specimens did not grow bacilli.

*F. H. Young*

LINCOLN, Edith M. & HOULD, F. **Results of Specific Treatment of Miliary Tuberculosis in Children. A Follow-Up Study of 63 Patients treated with Antimicrobial Agents.** *New England J. of Med.* 1959, July 16, v. 261, No. 3, 113–20.

Before the antimicrobial therapy era miliary tuberculosis was almost always fatal. Of 102 children with generalized miliary tuberculosis seen at the Bellevue Hospital, New York, between 1926 and 1944, 99 died within 1 year, and the remainder within 4 years. This paper deals with 63 patients with acute generalized miliary tuberculosis seen at the same institution between 1944 and 1956. In both groups the vast majority had evidence of primary pulmonary tuberculosis. The 2 groups presented with similar features. The tuberculin test was positive in 91% of the 165 patients. In 3 it was not done, and 2 patients were removed from the study as treatment was not persisted with through error.

Of the 61 treated patients, 6 of the first 9 who received thiazolsulfone [thiazosulphone; Promizole] survived, and none had meningitis. The drug was continued for 3 years (2 had streptomycin for short periods in addition). Renal tuberculosis in 2 and lung tuberculosis in 1 developed many years afterwards and were successfuly treated by the standard drugs. In the next group 29 patients received streptomycin in addition to the thiazosulphone; in 13 there was meningitis at some stage. 22 patients have survived at the end of 7 to 12 years. Of those who have died, 6 had meningitis, and 1 was moribund at the start of treatment. No late complication except one of phylctenular conjunctivitis developed subsequently.

In the 3rd group 25 patients received isoniazid, of whom 20 had streptomycin, and 24 thiazosulphone in addition. Clinical meningitis did not occur, but tubercle bacilli were recovered from the cerebrospinal fluid in 2. Cervical adenitis and otitis, phylctenular conjunctivitis and spondylitis occurred in 3 patients respectively during treatment, and tuberculosis of the femur in 1 after the completion of treatment. Only 1 patient died, 12 days after admission with very advanced disease. The X-ray picture of mottling in the lungs persisted for much longer when thiazosulphone was given alone.

*F. H. Young*

WRIGHT, N. L. **Treatment of Tuberculous Meningitis.** *Quart. J. Med.* (n.s.) 1959, July, v. 28, No. 111, 449–58.

In support of the view that it may be unnecessary to give streptomycin intrathecally in the treatment of tuberculous meningitis Wright presents the results of the analysis of the immediate and remote results obtained between 1947 and 1955 in 207 patients treated in a Belfast hospital.

The patients fell into 3 treatment groups and selection was determined only by date of admission in that the best available treatment at the time was used in each case. Streptomycin came into use in August 1947 when the series studied began.

The groups were:

I. those given streptomycin intramuscularly and intrathecally (120)
II. those given dihydrostreptomycin intramuscularly and intrathecally (33)
III. those given streptomycin intramuscularly and also (usually) PAS or isoniazid or both (54)

A few patients received additional drugs: 8 were given heparin (1948), 26 streptokinase (1949–51) and 4 intrathecal PPD (1950). During a 13-month period in 1950–51 dihydrostreptomycin was given as above.

After the introduction of isoniazid in 1952 the intrathecal administration of streptomycin was given up and treatment followed as in group III above.

Although as stated the groups of patients were not controlled their homogeneity has been tested in retrospect as far as concerned severity and duration of illness, state of cerebrospinal fluid, age and sex, presence of coexistent tuberculous lesions, place of origin, the presence of tuberculosis or a history of previous tuberculosis in the family and the patient's social class.

There was a significant preponderance of milder disease in group III accompanied by a higher level of sugar in the cerebrospinal fluid. The incidence of combined miliary and meningeal lesions was significantly greater in group III than in group I, though not greater than in group II. No other significant differences were found. Allowance for the significant variables was made in the final calculations.

The survival rate in group III was significantly higher than in group I; it was lowest in group II. Since other factors were eliminated the conclusion reached was that streptomycin given intramuscularly and combined with oral isoniazid or PAS or both is the best treatment of tuberculous meningitis. Intrathecal streptomycin is therefore not only unnecessary but is actually contraindicated because of its untoward effects and the distress which attends its administration.

The 94 survivors have been kept under supervision. Some are entirely free of any residual manifestation of the illness but others have been left with a recognizable

defect. The survivors of group III had fewer residual defects than those of group I and the difference was great enough to be significant. There were not enough survivors in group II for comparison. It was therefore concluded on this score also that intrathecal streptomycin is not necessary and that the best treatment of tuberculous meningitis consists of intramuscular streptomycin combined with oral isoniazid or PAS, or both. [See also this *Bulletin*, 1959, v. 34, 623.]

*H. G. Calwell*

WILKINSON, M. C. **Treatment of Tuberculosis of the Spine.** *Brit. Med. J.* 1959, Aug. 29, 280–82.

In Great Britain bone and joint tuberculosis is becoming much less common as infection is being eradicated from the dairy herds.

The author gives the results of his treatment of spinal tuberculosis in the pre-antibiotic era, for comparison with later results. In 40 of 51 patients where the disease was in the lumbar region the result was good, but in only 37 of 75 suffering from disease in the thoracic region a similarly good result was obtained.

From 1948 to 1958 inclusive 138 operations were performed on 128 patients under antibiotic cover given for about 4 months. Of these, 1 emigrated, 1 died of pneumonia, and 1 of tuberculous meningitis later, leaving 125 fully followed up. There were no operative deaths. 82 lesions achieved bony ankylosis, 40 stable fibrous ankylosis and 8 unstable fibrous ankylosis. The less favourable results previously reported in the thoracic region lesions did not continue in the present series. Where it was thought that operation was unnecessary 8 had unstable ankylosis and 97 satisfactory ankylosis, though the prognosis was worse in the thoracic cases. 21 patients had relapses, but 20 have been re-treated with satisfactory results. Some details are given about the operations used.

The paper gives convincing evidence that tuberculosis of the spine is now a very treatable disease.

*F. H. Young*

GROTH-PETERSEN, E., KNUDSEN, J. & WILBEK, E. **Epidemiological Basis of Tuberculosis Eradication in an Advanced Country.** *Bull. World Health Organization.* Geneva. 1959, v. 21, No. 1, 5–49, 26 figs. [56 refs.]

The steady decrease in all the tuberculosis indices, as a result both of natural causes and antimicrobial treatment, during the past few years in countries where the antituberculous campaign has been pursued diligently calls for a fresh appraisal of the methods necessary for the drive to eradicate the disease. These are different from those applicable to countries where the indices are still high. Denmark is an example of a country with decreasing tuberculous indices.

This report is divided into 3 sections. The first discusses briefly the main indices of tuberculosis and outlines the tuberculosis situation in Denmark during the past several decades, as a background to the work of the Danish Tuberculosis Index. The purpose of the second section is twofold: (1) to describe how the Danish tuberculosis mass campaign of 1950–52 was planned both as a community health service and in the interests of research; and (2) to set forth the findings of the campaign as far as they may be of interest in the follow-up studies. The final section is concerned solely with the new cases of tuberculosis appearing over the subsequent 4-year period in the adult population who were deemed healthy with regard to tuberculosis at the time of the campaign.

The present state of affairs in Denmark is described and the impossibility of comparing figures from various countries owing to differences of reporting and registration. In Denmark a positive reaction to 5 TU or 10 TU of purified tuberculin can be accepted as indicating infection, apart from BCG inoculation reactors. By 1952, 30–35% of the population had received BCG. The percentage of unvaccinated reactors rises from about 20% at the age of 20 to 80–90% at the age of 50. In 1956, 1,127 new cases of tuberculosis in a population of about 4,400,000 were notified, in whom 90% had tubercle bacilli recovered from their sputum. A series of graphs are given showing various aspects of this state of affairs.

The Danish mass campaign of 1950–1952 is then described. Of a census population of 2,080,000, some 795,000 were examined by tuberculin test to 10 TU and by photofluorograms and X-rays where indicated. BCG was offered to non-reactors and those whose reaction was less than 6 mm. It is notable that about 18% of those who had documented BCG inoculation gave negative readings. About the same number of new cases were disclosed as had been notified in the previous year, but there were half as many in the 15–24 age-group and more than 50% more in the 45+ age-group.

The third section examines the mass campaign results and tries to find which groups of examined population are likely to produce a high intake of new cases and which are relatively unimportant. Of the 795,000 adults examined 744,261 were regarded as free from tuberculosis. Of these, 878 developed tuberculosis during the following 4 years; 742 had pulmonary tuberculosis. The rate, 25 per 100,000 for pulmonary tuberculosis at all ages, was greater in the 15–34 age-group than the 35–45 + group. It was 5–8 times greater in the unvaccinated tuberculin-negative group than the vaccinated. 76% of the new cases came from the naturally tuberculin positive group. The high risk groups are defined; the major group is of those with abnormal shadows of various kinds. Especially in the younger age-groups, a pronounced tuberculin reaction suggests a high risk of developing tuberculosis later. It is suggested that persons in the older age-group with completely normal X-ray pictures, even with a positive tuberculin reaction, do not need regular annual X-ray examination. Efforts should be concentrated on those with abnormalities of any kind in the X-ray, and young people with large tuberculin reactions.

[This admirable study is given with a wealth of statistical tables and details which are too numerous to abstract. It will repay the most careful study by those who have to direct antituberculous campaigns.]

*F. H. Young*

OFFICIAL RECORDS W.H.O. No. 96. Executive Board Twenty-Fourth Session, Geneva, 1 and 2 June 1959. Annex 3. **Review of BCG Vaccination Programmes. Preliminary Report by the Director-General.** pp. 19–50, 2 charts. [Numerous refs.] 1959, Oct. Geneva: Palais des Nations.

This informative and well documented review of BCG vaccination presents an account of some of the recent literature on the subject, most of which has already been noticed in the *Bulletin*, and detailed statistics of vaccination campaigns carried out in 41 countries and territories between 1951 and 1958.

The degree of protection conferred by BCG vaccination has been examined in 4 "scientifically planned and conducted studies". The trial in North American Indians by ARONSON *et al.* showed that tuberculosis morbidity was reduced by about 75% over a period of 11 years [this *Bulletin*, 1958, v. 33, 943]. The British Medical Research Council's trial [*ibid.*, 1956, v. 31, 621] dealt with adolescents in a highly industrialized society, and the results over an average period of 4 years showed that the incidence of tuberculosis in the vaccinated group was only about 1/5th of that in the concurrent control group.

The United States Public Health Service conducted a trial in Puerto Rico. The first 6 years' follow-up showed that vaccination reduced the incidence of tuberculosis among the non-reactors from 43·2 per 100,000 to 29·2, a reduction of about 31%. The same body conducted another trial in the southern part of the United States in which vaccination was done by multiple puncture. The case-rate among the controls was 22·4 per 100,000 and that in the vaccinated 14·4. This difference was not statistically significant. There was reason to believe that the vaccine used in the second trial was lacking in potency, as witness the very low conversion rate observed at retesting 2 years after vaccination.

Certain well known reports on the effectiveness of BCG vaccination in comparable groups, where there was no planned procedure or random selection, are presented as giving circumstantial evidence. They include those of HYGE [*ibid.*, 1957, v. 32, 27], ENELL [*ibid.*, 1956, v. 31, 139], DAELEN *et al.* [*ibid.*, 1953, v. 28, 391] and SULA [*ibid.*, 1957, v. 32, 658]. From this and other evidence there is general agreement that the degree of protection afforded by BCG vaccination is of the order of 80%, which means that, in people considered eligible for vaccination, 5 times as many cases of tuberculosis will develop in the following years among unvaccinated persons as among the vaccinated.

Much evidence has been accumulated that the protection conferred relates not only to manifestations of primary or childhood types of tuberculosis but also to reinfection or adult types of pulmonary tuberculosis.

The relationship between post-vaccinal tuberculin sensitivity and protective effect is not direct but there is evidence both from animal experiments and from controlled trials in man that where a high degree of sensitivity develops a high degree of protection can be expected. Reports from internationally assisted campaigns show that there are considerable variations in the degree of post-vaccinal sensitivity in different countries and in the same countries at different times. This will be studied further.

With a single intradermal administration of the vaccine there remain two variable factors which influence the degree of protection. BCG is a live vaccine and cannot be standardized. Its bacillary count falls rapidly and great care must be taken in storage. Dried vaccine is much more stable than liquid but even at the best only 10–20% of the original bacilli will remain alive when the vaccine is being used.

The other variable factor is the criterion by which people are selected for vaccination. There is evidence that low-grade tuberculin sensitivity indicates a certain degree of protection acquired naturally and when, as at present, those with such sensitivity are accepted for vaccination it is not certain what additional protection BCG gives.

The inconveniences and risks of BCG vaccination are considered at length and it is concluded that they are not great. There is a risk of fatal disease in not more than 1 in a million. The disadvantages in relation to the epidemiological and diagnostic uses of the tuberculin test are discussed. The practical use made of the test varies and in most countries it is used so little that there is no argument on this ground against BCG vaccination. As a diagnostic test it is most often used in children in the early years of life. Vaccination at school-leaving age would not interfere with this use.

The statistical tables appended convey the impressive message that by the end of 1958 approximately 234 million persons had been tuberculin-tested and 88 million vaccinated in the entire programme.

*H. G. Calwell*

LITHANDER, A. **Investigation of the Tuberculin Allergy in Guinea Pigs after BCG Vaccination and after Subsequent Infection with Virulent Tubercle Bacilli.** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No 1, 80–92, 7 figs.

Sensitivity to tuberculin persisting for a considerable time after BCG vaccination may be due to the continuing effect of the vaccine or to subsequent infection with virulent tubercle bacilli. If it were found that the skin reaction to BCG tuberculin (the centrifuged substrate of a fluid culture) exceeded that to Old Tuberculin it is possible that the quantitative difference between the reactions might decide which was the case. The experimental work presented in this paper is a contribution to the solution of the problem.

The results of Mantoux tests with BCG tuberculin and OT were studied at intervals in guineapigs that had been vaccinated with BCG and become reactors to both tuberculins. The doses of vaccine in each of 3 groups was 0·15, 1·5, and 15·0 mgm. respectively.

13 weeks after vaccination it was found that 1 mgm. of OT elicited positive reactions about as often as did BCG tuberculin. With a dose of 0·5 mgm., however, positive reactions were obtained more often with BCG tuberculin than with OT.

In subsequent tests differences were found between reactions to BCG tuberculin and OT. With 1·0 mgm. of BCG tuberculin there was little difference in the frequency of positive reactions in all 3 groups up to 20

weeks but with 1·0 mgm. of OT a marked decrease in the frequency of positive reactions was seen as early as 20 weeks after vaccination, which progressed as time passed.

With 0·5 mgm. of BCG tuberculin there was a gradual decrease in the frequency of positive reactions from 20 up to 40 weeks in all 3 groups. With 0·5 mgm. of OT there was a marked decrease in the frequency of positive reactions. The decrease was considerable in the latest tests but least pronounced in the animals which had received the largest dose of BCG vaccine. This shows that in guineapigs post-vaccinal sensitivity can be better demonstrated a long time after vaccination by testing with BCG tuberculin than with OT.

Tuberculin sensitivity produced by BCG vaccination wanes with time, and when it falls to a certain low level it is more readily detected by BCG tuberculin, which is more specific than OT. In the last post-vaccinal tests (usually at 40 weeks) a considerable proportion of the reactions to 0·5 and 1·0 mgm. of OT were negative while reactions to 1 mgm. of BCG tuberculin were predominantly positive, and those to 0·5 mgm. were positive in about one-half of the animals.

When the vaccinated animals were infected with virulent tubercle bacilli immediately after the final post-vaccinal test later tuberculin tests showed a gradual increase in the frequency of positive reactions to OT and a decrease up to 5 weeks followed by a slight increase in reactions to BCG tuberculin. This led to an equalization of the frequency of positive reactions to both tuberculins.

It is possible that the course in man resembles that in guineapigs; so if in a person vaccinated with BCG positive reactions to both tuberculins are obtained at first, and reactions to OT become negative later while those to BCG tuberculin remain positive, and later still the reaction to OT shows an increase, this could give reason to suspect infection with virulent tubercle bacilli.

*H. G. Calwell*

OBAYASHI, Y., SAWADA, T., KUCHIKI, G., CHO, C., KAWASAKI, J. & OTA, S. **Studies on Correlation between Viability of BCG Vaccine and Tuberculin Allergy induced by Vaccination in Humans.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1151–64, 7 figs.

The degree of immunity conferred by BCG vaccination cannot be estimated directly but must be assessed by indirect criteria—among them tuberculin sensitivity, whose intensity and duration are regarded as indicators of the success or otherwise of vaccination.

It is generally accepted that the production both of tuberculin sensitivity and immunity depends largely upon the viability of the bacteria in the vaccine, and it was the object of the experiments described in this paper to determine whether and to what extent this is so.

In the first experiment schoolchildren, not previously vaccinated with BCG and who did not react to tuberculin or reacted only with erythema of less than 9 mm. to 5 TU of OT, were vaccinated with 0·05 mgm. of dried sucrose or glutamate BCG vaccine. On the day of vaccination culture tests were carried out on the vaccines used.

Post-vaccinal tuberculin tests were done at 1, 3–4 and 12 months, the reactions were read at 48 hours, and the diameter of erythema recorded. The same test was used as before vaccination.

Graphical analyses were made of the relation between the number of viable particles in the vaccine and the mean size of the post-vaccinal tuberculin reaction. A positive correlation was found between the 2 factors at 1 month; there was still a high degree of correlation at 3–4 months.

In the second experiment dried glutamate and sucrose vaccines stored for 1 month at various temperatures (5, 30, 38·5 and 50°C.) were inoculated into 1,211 schoolchildren not previously vaccinated with BCG and who did not react or reacted only with induration of 9 mm. to 5 TU of Danish PPD. On each day on which vaccination was done the vaccine used was tested by culture.

Post-vaccinal tuberculin tests were done at 4 and 12 months with 5 TU of both Japanese OT and Danish PPD. Measurements of the erythema (with OT) and induration (with PPD) were recorded.

There was a definite correlation between the number of viable units and the mean size of the tuberculin reaction at 4 months and again at 12 months. Correlation was found both in the degree of erythema with OT and the induration with PPD.

The above correlation can be expected only when the degree of bacillary aggregation is similar for each batch of vaccine, and there is a possibility that it may hold only when the same strain of BCG is used.

If the borderline of viability is drawn at 10 colonies in $10^{-6}$ mgm. in the above study, the mean size of the tuberculin reaction induced by vaccination will be 15 mm. or more at 12 months with OT and 13 mm. or more with PPD. By this standard the dried glutamate vaccine used was effective after storage at 38·5°C. for 1 month and fell only a little short after storage at 50°C. for the same period. It was also potent after 1 month at 37°C. and fell only a little short after 3 months at 37°C. The authors recommend that stored dried vaccines be submitted to culture tests as a routine.

*H. G. Calwell*

OBAYASHI, Y., CHO, C., SAWADA, T., KUCHIKI, G., OTA, S. & KAWASAKI, J. **Further Studies on Effect of Storage at High Temperatures upon Allergenic Potency of Dried BCG Vaccine.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1165–74, 2 figs.

The authors describe experiments which were made to determine the effect of storage at high temperatures on the allergenic potency of dried glutamate and sucrose BCG vaccines.

For 6–8 months preceding the study the vaccines were stored at 5°C. They were then kept at various temperatures, 5, 30, 38·5 and 50°C. for 30 days, after which they were stored again at 5°C. until used.

The 1,211 schoolchildren inoculated had not been vaccinated with BCG previously and either did not react or reacted only with induration of less than 9 mm. to 5 TU of Danish PPD.

The children were in 2 groups, and the 4 kinds of each vaccine were used in rotation. In addition some of the children in the sucrose vaccine group were given glutamate vaccine in order to compare the responses with those in the other group. Thus in this sub-group 5 kinds of vaccine were used. On the days of vaccination the vaccine to be used was reconstituted and subjected to culture test.

Post-vaccinal tuberculin tests were done at 4 and 12 months with Japanese OT and Danish PPD. Each child was given duplicate Mantoux tests with 5 TU, and reactions were examined at 48 hours, the diameter of erythema and induration recorded and the presence of double erythema noted.

The culture tests showed that the number of viable units was a little larger in the glutamate than in the sucrose vaccine even before storage at high temperatures. After storage the difference in the number of viable units in the vaccines increased with rise in temperature.

The results of the tuberculin tests were analysed. With glutamate vaccine a decrease in allergenic potency was seen only after storage at 50°C. but with sucrose vaccine a decrease was already evident at 30°C. Storage of sucrose vaccine at 38·5°C. resulted in a comparatively small decrease in potency detectable only in the erythema factor after 12 months. Storage at 50°C. had a marked effect on the allergenic potency of sucrose vaccine. There was no significant difference in either vaccine in this respect after storage at 5°C. but the potency of the glutamate vaccine was consistently higher than that of the sucrose vaccine after storage at 30 and 38·5°C.

The tuberculin reactions in those vaccinated with sucrose vaccine stored at 38·5°C. were stronger than would have been expected from the results of culture tests. After storage at 50°C. the same tendency was seen but there was no significant difference after 4 months. The reactions at 12 months were stronger after glutamate than after sucrose vaccine.

There was correlation between the mean size of the vaccination scar at 4 months and the degree of tuberculin sensitivity. *H. G. Calwell*

FREERKSEN, E. Der Superinfektionsschutz bei der Tuberkulose. [**Protection against Tuberculous Superinfection**] *Deut. med. Woch.* 1959, Aug. 28 & Sept. 4, v. 84, Nos. 35 & 36, 1533–40; 1617–19, 1665–6, 18 figs. [23 refs.]

Experiments show that animals previously vaccinated against tuberculosis and later infected with a virulent strain of the tubercle bacillus live longer than unvaccinated controls. Protection against superinfection does not develop immediately after vaccination but in 2–6 weeks. Knowledge of the duration of this protection, especially of its strongest phase, is uncertain.

Different strains of vaccinating organisms differ in the speed with which they confer protection, for example H37Ra works more quickly than BCG but its effect wanes sooner. Within certain limits there is no clear connexion between dose and effect, and the degree of protection cannot be increased indefinitely by increasing the dose. It is of course possible to go below the effective dose.

Different strains of mycobacteria provide different degrees of protection. Saprophytes are ineffective but strains of reduced virulence, *e.g.* H37Ra and BCG give good protection. Highly virulent strains cause rapidly advancing tuberculosis in guineapigs and rabbits which does not protect against superinfection but rather aggravates it.

In mice the *subcutaneous* injection of a virulent strain does not cause generalized tuberculosis, and the same strain can be used for superinfection by *intravenous* injection. Experiments show that a highly virulent strain or the avirulent strain H37Ra confers a high degree of protection against bovine superinfection. A similar degree of protection is afforded by a virulent bovine strain and BCG against superinfection with a virulent human strain.

The strain used must be pathogenic if it is to afford protection. Saprophytes do not cause either local or generalized tuberculosis. On the other hand BCG causes a local "tuberculous" lesion which regresses; when injected intravenously or into the heart in large doses it can cause fatal tuberculosis in guineapigs. Saprophytes cannot do this.

The faculty of avirulent strains to produce a tuberculous lesion is part of the make-up of the bacillus whether alive or dead. Killed BCG can cause a typical regressive "tuberculous" focus in rabbits and guineapigs whereas killed saprophytes cannot do so.

Pathogenicity by itself does not enable mycobacteria to cause tuberculous disease. There must be in addition the power to multiply, which is virulence. An avirulent pathogenic organism can be rendered virulent as for example when large doses of BCG are injected intravenously, which may kill an experimental animal. This is not possible with non-pathogenic strains.

Killed pathogenic mycobacteria remain pathogenic but cease to be virulent. The addition of an adjuvant may render them apparently virulent by promoting prolonged contact between the host's tissues and the "pathogenic factors". In some such way fatal tuberculosis has followed BCG vaccination in a few vaccinated persons and BCG can cause tuberculosis in the golden hamster.

The question of the value of dead vaccines was examined. It is possible to protect against superinfection by a killed vaccine if the dose is large, the superinfection is not massive and an adjuvant is used with the vaccine to prevent too rapid elimination of the organisms and to retain them in prolonged contact with the tissues. Protection appears to persist only while the organisms themselves persist. Heterologous vaccines were found to be of little or no value.

As a result of experimental work it was concluded that in man existing active and inactive tuberculosis can be regarded as a kind of natural vaccination which protects against superinfection. Whether this is true of inactive tuberculosis has not in the author's opinion been proved experimentally. It will be remembered that there was experimental evidence of existing virulent infection aggravating later superinfection, which finding may cause speculation about the wisdom of mixing

patients with open and closed pulmonary tuberculosis in the same ward.

The fact that in some communities tuberculous disease occurs more frequently in known reactors than in persons hitherto non-reactors may be due to the same organic factors reactivating an inactive lesion as are responsible for it ceasing to have a protective effect.

No protective effect of any fraction of the tubercle bacillus could be demonstrated; the phosphatid fraction has been found to produce granulomata in tissue and although a protective effect has been described it has not been confirmed.

Sensitivity to tuberculin does not confer protection but it is of great importance and if its specificity could be exploited accurately enough it would serve for diagnosing the type of infecting organism without any bacteriological examination. Serological reactions are not specific nor do they measure resistance or even the activity or any other characteristics of tuberculous disease.

Tuberculin sensitivity is separate and different from immunity to superinfection. The mouse can be immunized successfully but does not become sensitive to tuberculin. and vaccinated animals can be desensitized without losing the protective effect of vaccination.

Tissue culture experiments indicate that protection against superinfection acts largely by improving the body's natural protective mechanisms and is not simply an immunological phenomenon.

The experimental results described support the claims for the value of BCG vaccination that are based on epidemiological studies in man. *H. G. Calwell*

HEISIG, F. Der Wert der Calmette-Schutzimpfung. [**The Value of B.C.G. Vaccination**] *Deut. med. Woch.* 1959, Sept. 4, v. 84, No. 36, 1620–25, 1667. [18 refs.]

The development of BCG vaccination in Germany was seriously retarded by the Lübeck disaster of 1929–30 when 72 vaccinated children died of tuberculosis. In spite of adequate proof that the vaccine had been contaminated by a culture of a highly virulent human strain of tubercle bacillus the shock to the public mind was so great that it was not until 1945 that BCG vaccination again became permissible by law.

In 1947 vaccination became widespread in Germany, and in 1948 voluntary mass vaccination was begun in the province of North Rhine-Westphalia (population 15,000,000) in the Federal Republic.

Vaccination is voluntary in the Federal Republic but in the Democratic Republic tuberculin testing is compulsory for children in their 1st, 4th and 8th years at school while vaccination can be refused on stated grounds agreeable to the school authorities. The rate of refusal in Germany is declining.

In the period 1948–58 808,365 persons were vaccinated in North Rhine-Westphalia; the vaccination was done by multiple puncture in 87,634 cases. The total does not include the newborn. Since the introduction of the multiple puncture method ulceration at the site of vaccination has practically disappeared.

The preliminary tests used are the patch test followed by the Mantoux test with 50 TU of OT. In the Democratic Republic a single test of 30 TU is used.

Whether or not to use BCG tuberculin instead of OT is not yet settled. It has not yet been shown that it is possible to differentiate without doubt between sensitivity due to BCG and that due to natural infection.

In a reported series of 26 infants vaccinated with BCG at birth it was found that 21 of them tested on the 10th day after vaccination were reactors to BCG tuberculin on the 17th day and 5 others who were retested reacted 2 days later. This demonstration of early conversion (and therefore of successful vaccination) argues against the need to isolate vaccinated infants from the source of infection for the usual period of 6 weeks.

In the Democratic Republic 79·8% of all newborn infants were vaccinated with BCG. It is pointed out that this could not have been achieved without the aid of nursing sisters, specially trained in tuberculin testing and BCG vaccination, who did the bulk of the work.

The safety of BCG is accepted by the author who discusses the 4 BCG fatalities already reported in the world literature and the 15 cases of lupus. He concludes that BCG vaccination is the safest of the current immunizing procedures.

Many classical examples of the efficacy of BCG, already familiar to all interested in tuberculosis, and some contemporary reports from Germany are presented. There was a ratio of vaccinated to unvaccinated persons with tuberculosis of 1:10 in North Rhine-Westphalia, 1:21 in the Democratic Republic until 1955 (about 1·7 million vaccinations) and 1:34 in Dresden. Heisig calls for an extension of BCG vaccination in the Federal Republic in spite of the falling incidence of infection. *H. G. Calwell*

FINLAND, M. **Tuberculosis Mortality and Morbidity and the Problem of BCG Vaccination in the United States.** *New England J. of Med.* 1959, Oct. 1, v. 261, No. 14, 699–702. [13 refs.]

DUBLIN [this *Bulletin*, 1959, v. 34, 425] has predicted a decline in the tuberculosis mortality rate in the United States of America to 1·3 per 100,000 by 1967 and to 0·3 by 1975. In view of this prediction Finland examines some divergent views on BCG vaccination among experts in the United States.

In 1957 an advisory committee of Research Foundation, Chicago [this *Bulletin*, 1957, v. 32, 946] argued strongly in favour of the vaccination of infants and children in areas of high incidence of tuberculosis and of specially exposed persons such as contacts and medical personnel.

In 1958 PALMER *et al.* [this *Bulletin*, 1959, v. 34, 879] reported that in community trials in Puerto Rico and Georgia and Alabama vaccination could have reduced the total amount of tuberculosis in the study population only by less than 10%.

They concluded that where infection rates are low the clinical complications of vaccination, however uncommon. might counterbalance the gains derived from preventing a few cases of tuberculosis. The most important disadvantage, however, would be the loss of the tuberculin test in diagnosis and epidemiology.

They therefore found against the extensive use of BCG vaccination in the United States; it is added that CARROLL *et al.* [no reference given] commented that the use of the vaccine in nurses, medical students, laboratory workers and contacts implies a situation in which present-day control methods cannot be applied satisfactorily.

In 1959 ANDERSON *et al.* presented the case against BCG [this *Bulletin*, 1959, v. 34, 881]. Further comment on this would be superfluous. BADGER (*New England J. of Med.*, 1959, v. 261, 131) "although obviously lacking enthusiasm for the use of BCG, is not quite willing to urge its complete abandonment" in the United States. He believes that the use of BCG vaccination and tuberculin testing are antagonistic procedures in the same community, and one plan or another, but not both should be adopted.

*H. G. Calwell*

CALWELL, H. G. **B.C.G. Vaccination.** [Correspondence.] *Brit. Med. J.* 1959, Aug. 29, 300–301.

Calwell's letter is an answer to the paper by ANDERSON *et al.* [this *Bulletin*, 1959, v. 34, 881] in which those authors throw considerable doubt on the value of BCG, and indicate that equally good results in the control of tuberculosis can be obtained without it if certain well known steps are taken. Calwell points out that this is not the opinion of the American Trudeau Society, the Medical Advisory Committee of Research Foundation, and other responsible organizations in the United States and elsewhere, and that Anderson and his colleagues, who are not basing their case on any new evidence or on their own experience, are therefore not speaking for the United States in this matter.

Calwell appreciates the value of the steps (which do not include BCG) taken by MYERS and his colleagues in protecting medical students and other hospital personnel. He quotes figures from other communities which show that there are still places in the United States where infection is common, and he urges that if BCG were used in these communities the infection rates would be reduced. *Charles Wilcocks*

NORTH, J.; RANGANATHAN, K. S. & SANJIVI, K. S. **B.C.G. Vaccination.** [Correspondence.] *Brit. Med. J.* 1959, Sept. 19, 499–501. [13 refs.]

*The Case Against B.C.G.* [this *Bulletin*, 1959, v. 34, 881] by 17 American physicians has provoked some highly critical replies of which the letter from Ranganathan and Sanjivi is a moderate and telling example.

The authors, writing from Madras, India, find fault with the American critics of BCG vaccination for ignoring objective proof that BCG confers ability to destroy tubercle bacilli rapidly at the site of infection [STRÖM, *ibid.*, 1956, v. 31, 138], and for their scant consideration of the first report of the Medical Research Council's Tuberculosis Vaccine Trials Committee [*ibid.*, 1956, v. 31, 621].

The American physicians' disparaging reference to mass vaccination campaigns as puzzling because time, effort and funds are spent upon non-reactors to tuberculin has no appeal for Ranganathan and Sanjivi, who are fighting tuberculosis in India were "almost 75% of the children become reactors to 5 TU PPD before the age of 15 years". In these conditions the loss of the tuberculin test as a diagnostic technique matters little. Madras is not Minnesota.

Neither are the Indian physicians consoled to learn from their American colleagues that the immediate prognosis of the tuberculosis of the first infection type is excellent either in the absence or presence of treatment since in a study made by one of them in Madras [this *Bulletin*, 1940, v. 15, 102] it was found that the death rate under the age of 10 among 1,947 children born to tuberculous patients was more than 8 times that for children under 10 in the general population, although the causes of individual deaths could not be verified.

"For the over-populated and under-developed countries with their totally unsatisfactory organization of medical facilities, the precedent established by Myers in the application of tuberculin testing and rigid contagious disease technique for the control of tuberculosis has little practical value. The immense magnitude of the tuberculosis problem in under-developed countries, the lack of adequate financial and other resources, and the evidence that B.C.G. vaccination can confer a substantial degree of protection and reduce the incidence of tuberculosis in those uninfected justify the continued administration of B.C.G. on a mass scale as a short-term measure, but not to the exclusion of recognized fundamental control measures."

The letter from North (who writes from New Zealand) contains information on the incidence of tuberculosis in the nursing staff of a hospital before and after the initiation of BCG prophylaxis for tuberculin-negative persons in 1948. The figures show a dramatic sudden fall which North feels is significant.

*H. G. Calwell*

GEMMILL, J. S. **BCG Vaccination. Complications at Different Ages.** *Med. Officer.* 1959, Sept. 18, v. 102, No. 12, 141–6, 2 figs. [32 refs.]

This paper gives an account of the complication of BCG vaccination seen in 19,720 newborn infants vaccinated in 5 Glasgow hospitals in the period 1952–56. They were non-contact infants. The dose used was 0·1 ml. of fresh Danish vaccine given intracutaneously.

The total number of complications was 329 (1·67%) in 295 infants. 85% of the complications were glandular; polyp formation of granular tissue occurred at the site of vaccination in 3 infants and abscess at the site in 46.

Regional adenitis occurred as follows: axillary 232, cervical 31, subclavicular 6, and in 11 infants there was enlargement of a gland in the upper arm between the vaccination site and the regional glands. Abscesses of the glands developed in 204 cases of the 269 cases of regional adenitis (76%) and spontaneous resolution in 65 (24%). Some abscesses remained static for months or years. The pus evacuated was thin, creamy, caseous or dense-solid.

The highest incidence of regional adenitis was found in the second month; in 197 cases (73%) the complication occurred within 4 months and in 242 (90%) within

6 months of vaccination. In 6 the onset was delayed for over 1 year after vaccination.

112 random specimens of pus were examined bacteriologically. "BCG was recovered in 62·5%." [The evidence for this difficult identification is not given.] Other organisms, presumed to be contaminants, were found in 8 specimens.

Incision is recommended as the only satisfactory method of dealing with gland abscesses. It should not be considered for at least 6 weeks (after the condition is detected) unless clearly inevitable. Chemotherapy is not indicated except for rare complications such as lupus.

The above incidence of complications was compared with that in 23,961 children aged 13 years who were vaccinated in 1953–55. The rates were 1·67% and 0·12% respectively. 85% of the infant complications were glandular and 83% of those in the schoolchildren papular at the site of vaccination.

Gemmill recommends that vaccination should be done in the depression of the deltoid anteriorly and not in the centre line of the arm where there is greater likelihood of trauma and whence the lymph drainage is unpredictable in direction.

There is much evidence that local abscess formation is due to deep injection but when it is seen that local abscesses are relatively rare in infants, in whom strictly intracutaneous injection is presumably more difficult than in older children, a more reasonable conclusion is that age is a more important factor than technique.

The facts given support the view that if vaccination were postponed until at least the age of 6 months the incidence of adenitis would be relatively low, but there are good reasons for not advancing the age of vaccination, among which are the accessibility of the newborn in hospitals and the absence of the necessity to do a preliminary tuberculin test.

Any proposal to reduce the dose of vaccine must be considered in relation to the duration of subsequent immunity. Freeze-dried vaccine is being tried by the author on a limited scale. [The standard Danish vaccine used above contains 0·075 mgm./0·1 ml. of BCG. The State Serum Institute of Copenhagen also issues "R" vaccine which contains 0·0375 mgm./0·1 ml. The reviewer has used this in infants for some years and found it satisfactory.] *H. G. Calwell*

ALVSAKER, J. O. **Erythema Multiforme following B.C.G. Vaccination.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, No. 3, 221–6. [13 refs.]

A girl aged 16 years developed erythema multiforme simultaneously with a Koch's phenomenon 1 week after revaccination with BCG. She had never previously suffered from skin disease or allergic disorder.

In 1955 she did not react to a Von Pirquet test and was vaccinated with BCG intracutaneously; she was revaccinated in 1957. In 1958 the girl reacted to the von Pirquet test with induration and erythema of 1 mm. She was therefore vaccinated with BCG a third time.

One week after the last vaccination an exanthem arose suddenly on her brow and face and spread within 10 days to the arms and trunk. Simultaneously ulceration with yellow discharge appeared at the site of vaccination.

The skin eruptions were multiform. No tubercle bacilli were seen in biopsy tissue. A few days after the skin excision there was an ulcer at the site similar to that at the site of vaccination on the leg.

Bacteriological examination revealed neither streptococci in the throat nor tubercle bacilli in the stomach residue. Guineapig inoculation of material from the ulcers was negative. The contents of the vesicles and pustules were sterile.

There was no evidence of skin allergy to Sauton's medium but a von Pirquet test was positive.

The antistreptolysin titre was raised during the course of the illness, probably due to a chronic streptococcal infection in the teeth.

There was no evidence of tuberculosis in the patient or her environment, and the supposition is advanced that a streptococcal infection along with the BCG infection had provoked an allergic reaction, *viz.* erythema multiforme. The negative von Pirquet test before the 3rd vaccination does not exclude a certain degree of tuberculin sensitivity leading to the Koch phenomenon.

*H. G. Calwell*

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## VENEREAL DISEASES

DUXBURY, A. E. & LAWRENCE, J. R. **Primary Venereal Herpes Simplex Infection in the Male.** *Med. J. Australia.* 1959, Aug. 22, v. 2, No. 8, 250–52. [18 refs.]

This is an account of a case of herpes simplex where the infection was acquired venereally and the penile vesicle was the primary lesion. The virus was isolated from the blister or vesicle fluid by culture in baby mice and identified by neutralization tests with the mouse brain suspension. The patient's serum showed a 22-fold increase in neutralizing antibody between the acute phase and the convalescent phase of the disease.

*H. J. Bensted*

BRITISH J. VENEREAL DIS. 1959, June, v. 35, No. 2, 71–110, 13 figs. [Numerous refs.] **Symposium on Reiter's Disease.**

This disease is dealt with at considerable length in a series of 7 articles by different authors. The last, which might well have been placed first, is entitled *Reiter's disease* by H. BAILEY and W. J. BISHOP (pp. 101–102); this gives a short biography of this famous man who first described the disease in 1916, together with photographs of Reiter himself and of Leipzig University of which he was a gold medallist.

The articles under consideration include *Ankylosing*

*spondylitis* by R. M. MASON (pp. 71–76), *Significance of sacro-iliitis in Reiter's disease* by G. W. CSONKA (pp. 77–80), *Reiter's disease and ankylosing spondylitis* by J. K. OATES (pp. 81–83), *Bacteriological and biochemical investigations in Reiter's syndrome* by G. W. CSONKA (pp. 84–88), *Incidence of genital infection in male patients with ankylosing spondylitis* by J. K. OATES (pp. 89–91), and *Pelvic infection as a cause of bilateral sacro-iliac arthritis and ankylosing spondylitis* by R. G. GRAINGER and C. S. NICOL (pp. 92–98); these were followed by a discussion in which 11 persons participated.

The classical signs of Reiter's disease consist of urethritis, arthritis and conjunctivitis but all of these are not necessarily present in every patient; the arthritis usually attacks peripheral joints but often affects the sacro-iliac joints and in this respect has points in common with ankylosing spondylitis; this latter occasionally starts in the joints of the lower limbs and may be accompanied by iritis but must not be diagnosed in the absence of radiological evidence of sacro-iliitis; it should be distinguished from rheumatoid arthritis and rheumatic fever; it may occur in association with psoriasis and ulcerative colitis (especially dysentery); as a rule sacro-iliitis occurs early in ankylosing spondylitis and late in Reiter's disease.

For the treatment of ankylosing spondylitis radiotherapy has had many supporters but the danger of leukaemia must be remembered and often the effect is merely palliative; barbiturates and physiotherapy will usually give equally good results. It is of interest to note that some form of genital infection, especially chronic prostatitis, is commonly found in patients with ankylosing spondylitis, as in Reiter's disease, but whether this is the cause or not is by no means clear; more than one observer has noticed a familial factor, which is not seen in Reiter's disease.

Csonka examined 134 patients with Reiter's disease and found evidence of sacro-iliitis in 27 (20·1%); when those with and without sacro-iliitis were compared with those with ankylosing spondylitis, points of difference—age and sex incidence, type of onset, proportion of peripheral joint and spinal involvement and incidence of iritis—were greater between ankylosing spondylitis and Reiter's disease with sacro-iliitis than the points of similarity and he concludes that these are 2 separate diseases; he too noticed no familial tendency in Reiter's disease. Oates inclines to the view that these 2 diseases both commonly show evidence of genital infection, particularly chronic prostatitis; however, since various observers have reported prostatitis in 17–35% of normal males and he found 20% in normal males compared with 33% in those with rheumatoid arthritis, the role of prostatitis seems doubtful. He sets out a list of 10 points of similarity between the 2 diseases and 4 in which they differ; typical cases of each disease are easily diagnosed but he suggests that there may be a common infective agent, the effects of which vary according to genetic disposition, tissue response, site and mode of infection and the effect of repeated infection.

Csonka carried out a number of investigations, bacteriological and biochemical, in 211 patients with Reiter's disease; PPLO were found in 11·8% of patients with this disease, in 2·1% of healthy persons and in 46·9% of those with non-specific urethritis; gonococci were found in 107 out of 195 cases and the gonococcal complement-fixation test was positive in 66 out of 168 cases; pus cells were found in the prostatic secretion of 55% of 132 patients; a moderate normocytic anaemia was found in 15·9% and 33% showed some leucocytosis; the sedimentation rate was usually raised in the presence of active disease; serum tended to show a decrease in albumin and an increase in the alpha globulins roughly parallel with the severity of the disease; the gamma globulin was only slightly raised; the differential agglutination test was usually negative, LE cells were not found, C-reactive protein was rarely present as was serum uric acid.

Oates found that 84% of 72 males with this disease had chronic prostato-vesiculitis and 9 suffered from non-specific urethritis; of 82 males 9 gave a history of gonorrhoea, 3 of non-specific urethritis and 8 had had urethritis; he considers that treatment and follow-up of all patients with a genital infection is indicated.

Grainger and Nicol discuss the diagnosis of Reiter's disease and show 7 radiographs illustrating the bony changes which take place in the heels, hands and sacro-iliac joints in cases of non-specific urethritis (? Reiter's disease), and in the sacro-iliac joints in ulcerative colitis and in ankylosing spondylitis. They consider that pelvic infection is a common cause of sacro-iliac disease and probably also of ankylosing spondylitis; the one may herald the approach of the other.

In the discussion which followed the reading of these papers considerable differences of opinion were expressed but there was some agreement that non-specific urethritis was usually venereal in origin and that both Reiter's disease and ankylosing spondylitis were probably infective processes. The most remarkable point was that the disease rarely occurred in females.

*T. E. Osmond*

BRITISH MED. ASS.: Venereologists' Group Committee, in association with the BRIT. CO-OP. CLIN. GROUP. **Treatment of Venereal Disease outside the Hospital Service.** *Brit. J. Venereal Dis.* 1959, June, v. 35, No. 2, 111 15.

In order to find out how many patients with venereal disease are being treated outside the hospital service [presumably public clinics is meant], the BMA sent out a questionnaire to 1,743 doctors in 4 selected areas—Kensington and Hammersmith, Leeds, Norfolk and Southampton; only 562 rep'ied and of these only 109 admitted treating venereal disease; these included 92 general practitioners and 17 specialists, not necessarily venereologists. Patients treated included 56 with syphilis, 97 with gonorrhoea, 224 with non-gonococcal urethritis and 78 with "other VD"; of these 455 patients 275 were treated under the National Health Service and 180 privately.

It is calculated that if patients with VD treated outside the public health service were added to those reported by clinics there would be a rise of 1/4 for syphilis and 1/7 for gonorrhoea and non-gonococcal urethritis. Details are set out in 5 tables and an appendix.

It is generally agreed that a percentage of patients treated for venereal disease is not included in the official figures issued by the Ministry of Health but what that percentage is is not known, nor is it likely to be; this report does not seem very enlightening, since only 562 replies were received from 1,743 persons questioned. What might be helpful would be to send questions to known venereologists. [Incidentally "hospital" and "clinic" seem to be used synonymously; some patients with late syphilis, for example, are treated in hospital wards or out-patient departments and would therefore, presumably, not be included in the official figures.] *T. E. Osmond*

CRAPS, M. Règlements, législation et contributions médico-sociales belges dans le domaine de la lutte antivénérienne depuis la fin du XVIII[e] siècle jusqu'à nos jours. **[Regulations, legislation and socio-medical contributions in Belgium in the Control of Venereal Disease from the end of the 18th Century up to the present time]** *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1959, July, v. 17, No 7, 477–505. [56 refs.]

The authors of this very long article divide their subject into 4 periods: (1) 1791–1918, (2) 1919–1940, (3) 1941–1948 and (4) 1949–1958.

In the first period laws gave police the right to enter at any time premises known to be centres of debauchery, and regulated prostitution. During the later periods venereal dispensaries and free treatment were introduced; from 1914 the German invasion was followed by compulsory notification, naming sources of infection by the military and strict police observation; nevertheless venereal disease increased enormously.

In the second period an antivenereal programme was undertaken by the Ministry of Health and effective treatment greatly reduced the number of contagious persons; after 1925 financial stringency reduced the money available for diagnosis and treatment at clinics and the incidence of venereal disease rose, to fall again by 1940.

In the third period German invasion again caused the introduction of measures against venereal disease, which nevertheless increased considerably; towards the end of this period regulation of prostitution was discontinued.

In the fourth period treatment of the infected and search for contacts were the key notes of policy.

Details of the various laws and regulations are given in the text but cannot be reproduced in an abstract; regulation of prostitution may have been suppressed but prostitutes have not. The authors conclude that legislation may *appear* to be satisfactory but it is not the letter of the law which matters but the way in which it is applied. *T. E. Osmond*

KING, A. J. & CATTERALL, R. D. **Syphilis of Bones.** *Brit. J. Venereal Dis.* 1959, June, v. 35, No. 2, 116–27, 30 figs. [29 refs.]

Syphilis of bones is less common than formerly for obvious reasons; it may occur (1) during or after the secondary stage, (2) after the third year, (3) early or late in congenital syphilis.

(1) This shows itself as osteocopic pains and headache but radiological changes are not usually visible; acute osteomyelitis of the long bones and osteolytic areas in the skull have been reported. (2) In late syphilis gummata of bone occur with periostitis and much new bone formation which is very hard, *e.g.* sabre-shaped tibia; on the other hand lesions may be mainly destructive, especially in the skull bones; serum reactions are nearly always positive. (3) In congenital syphilis there may be enlargement of the epiphyseal ends of bones, broadening and irregularity of the epiphyseal lines, sclerosis of zones of provisional calcification, irregular areas of osteoporosis, thin regular subperiosteal deposits of new bone and pathological fracture. Bony lesions are shown by X-rays in the first 3 months of life and intense periosteal reaction occurs in the second 6 months and new bone is laid down; in the late stages lesions are mostly of the gummatous type; dental radiographs are said to be of value in diagnosis especially those of unerupted teeth.

The great value of this article lies in the 30 beautifully reproduced radiographs which could hardly be bettered and well repay careful study. *T. E. Osmond*

HARRIS, A., SUNKES, E. J., BUNCH, W. L., Jr. & BOSSAK, H. N. **An Evaluation of the Plasmacrit "Screening" Test for Syphilis. Presented in part at the Tenth Annual Symposium on Recent Advances in the Study of Venereal Diseases, Baltimore, Maryland, April 27–28, 1959.** *Pub. Health Lab.* 1959, July, v. 17, No. 4, 83–7.

The Plasmacrit (PCT) test [this *Bulletin*, 1959, v. 34, 884] was carried out on heparinized blood obtained in capillary tubes from a finger prick; tubes were centrifuged at 11,000 r.p.m. for 3 minutes, the contents of a 20–26 mm. length were blown into a 14 mm. paraffin ring on a glass slide and one drop (0·01 ml.) of choline chloride antigen added; the slide was rotated and results read as in VDRL test. The plasma was unheated and the antigen the same as in VDRL but with the addition of choline chloride [amount not stated].

This test was carried out in parallel with VDRL on 599 presumably non-syphilitic sera and 109 presumably syphilitic sera.

In the former PCT was reactive in 6·7% and VDRL in 1·2%; in the latter the respective figures were 88·1% and 70·7%.

Thus PCT appears to be more sensitive but less specific than VDRL; it should be useful as a screen test in hospitals, blood banks, clinics or mass-testing programmes and especially where venepuncture is contra-indicated. *T. E. Osmond*

SIEFERT, G. Neue Untersuchungen über Antigenfraktionen der Syphilis-Spirochäte und ihre Bedeutung für die Lues-Diagnostik. **[New Studies on the Antigen Fractions of Syphilis Spirochaetes and their Importance in Diagnosis]** *Reprinted from Klin. Woch.* 1959, May 1, v. 37, No. 9, 519–23, 2 figs. [24 refs.]

In the introduction to the work described in this paper there is mention of the problems which still exist in the

classical serological diagnostic tests of syphilis and also some account of recent publications on the morphology and biochemistry of spirochaetes and leptospirae. The experimental work consisted of the extraction of the protein constituents from *Treponema pallidum* (Nichols strain) which had been cultured in rabbit testicle. This extract had a high serological activity in complement-fixation tests with anti-syphilitic rabbit sera. By means of paper electrophoresis the protein extract was found to be divisible into 5 fractions of which 3 were proved to be serologically active. *M. E. Delafield*

PAVLATOU, M., MARCELOU, U. & TRIANTAPHYLLI, I. L'antigène tréponémique—souche Reiter—dans la sérologie de la syphilis. [**Treponemal Antigen—Reiter Strain—in the Serology of Syphilis**] *Rev. d'Immunologie.* 1958, Apr.–June, v. 22, No. 3, 222–9. [31 refs.]

This article first gives a short review of various antigens which have been employed for this purpose.

The authors prepared an antigen from Reiter's spirochaete by centrifuging an 8-day culture, washing with normal saline and adding 0·3% phenol; the technique was Kolmer's complement fixation. 443 sera were tested in parallel by the TPI, Kahn, Wassermann and the Reiter complement-fixation (R) tests. The sera were from persons with syphilis or other diseases, pregnant women, leprosy patients, and others.

In 250 cases (223 negative and 27 positive) there was complete agreement; of 73 sera positive with TPI 54 were positive and 19 negative with R; 17 of these 19 were from patients with long-standing syphilis who had had intensive treatment; on the other hand 10 sera negative with TPI were positive with R and with classical tests; these were mostly from patients with diseases known to give false positive reactions.

In the 443 sera the R test was apparently falsely positive in 10 out of 147 (8·25%), compared with 33·18% with the classical reactions. Thus the R test was less sensitive and less specific than the TPI but gave far fewer false positive reactions than classical tests; it appeared to be somewhat less sensitive than these latter but should be useful when used in parallel with them in elucidating false positive reactions. If the antigen could be improved better results might be obtained.

*T. E. Osmond*

ANDERSON, R. I. & KENT, J. F., with the assistance of R. W. SANDERS, J. P. DUFFY, Suzanne MOORE, Lois A. SIMONTON & D. P. CARROLL. **Evaluation of the *Treponema pallidum* Immobilization Test of Serum and Cerebrospinal Fluid.** *Amer. J. Clin. Path.* 1959, Sept., v. 32, No. 3, 233–9. [24 refs.]

The TPI test and the VDRL slide and Kolmer complement-fixation tests (with cardiolipin antigen) were carried out in parallel on 1,302 sera and the TPI and Kolmer tests on 386 cerebrospinal fluids (CSF). Tests on syphilitic sera showed that adsorption with cardiolipin antigen removed all the antilipid antibody without affecting the immobilizing antibody.

Results of the parallel tests are set out in tables from which it can be seen that in primary syphilis 12 sera were reactive with lipid tests but non-reactive with TPI; in the later stages the two showed good agreement; treatment in the early stages affected the TPI more than the others but the reverse held in late syphilis.

Of 849 presumably non-syphilitic persons 3 were reactive and 10 weakly reactive with TPI compared with 70 reactive with lipid antigens; of these 70, 26 had infectious disease (principally leprosy) and 38 mostly showed evidence of "collagen" diseases.

In CSF from neurosyphilitic patients both types of test were usually positive; in those with syphilis but with no evidence of nervous involvement 13 were reactive with TPI but non-reactive with the other tests; 51 CSF from normal persons were negative with all tests.

This report confirms the belief that the TPI test is highly specific and also that immobilizing antibody is produced somewhat later than antilipid antibody.

*T. E. Osmond*

HEDERSTEDT, B. **A Comparative Study of the *Treponema pallidum* Immobilization (TPI) and the *Treponema pallidum* Complement Fixation (TPCF) Tests.** *Acta Path. et Microb. Scandinavica.* 1959, v. 45, No. 1, 62–6.

These 2 tests were carried out in parallel on 318 sera. The antigen for the TPCF was prepared from the testicles of irradiated rabbits; 10 rabbits produced sufficient antigen for about 1,000 tests; antigen kept well at −10°C.

Of the 318 sera 230 were positive, 4 weakly positive and 84 negative with the TPI test; the corresponding figures for the TPCF test were 148 or 188 (with dilutions 1/4 and 1/2), 12 and 24 (anticomplementary) and 158 and 105.

In no case was TPCF positive when TPI was negative.

Thus TPCF is considerably less sensitive than TPI though there is a possibility that this may not be so in early syphilis where TPI is frequently negative; TPCF is considerably simpler to perform than TPI but cannot replace it. [The status (syphilitic or not) of the 318 sera is not given.] *T. E. Osmond*

BEKKER, J. H. **Specificity and Sensitivity of the Reiter Protein Complement-Fixation (RPCF) Test. Report on 1,400 Selected Sera.** *Brit. J. Venereal Dis.* 1959, June, v. 35, No. 2, 129–31. [19 refs.]

This author compared the Reiter protein complement-fixation test (RPCF) with the TPI test on a number of syphilitic and non-syphilitic sera. Three techniques for the RPCF were used, (1) that described by DE BRUIJN [this *Bulletin*, 1958, v. 33, 945], (2) regular Kolmer with 2 full units of complement, and (3) Kolmer's technique with 1½ exact units of complement [*ibid.*, 1956, v. 31, 906.]

In series (1) of 145 syphilitic sera 142 were positive with RPCF and 135 with TPI test; of 155 non-syphilitic sera 4 were positive with RPCF and none with TPI; thus the relative sensitivities were 98 and 93% and the relative specificities 97·4 and 100%.

In series (2) of 368 syphilitic sera 347 were positive

with RPCF and 350 with TPI; of 377 non-syphilitic sera 8 were positive with RPCF and 2 with TPI; thus the relative sensitivities were 94·3 and 95·1 and the relative specificities 97·9 and 99·5%.

In series (3) of 187 syphilitic sera 185 were positive with RPCF and 179 with TPI; of 168 non-syphilitic sera 4 were positive with RPCF and none with TPI; thus the relative sensitivities were 98·9 and 95·7% and the relative specificities 97·6 and 100%. Overall, there was 95·3% agreement between the 2 tests; it appears that the sensitivity of the RPCF is greatly increased by using the technique employed in series (3).

The Reiter protein antigen is probably a lipopolysaccharide-protein complex [*ibid.*, 1959, v. 34, 494]; the antibody which reacts with the protein differs from reagin and also from immobilizing antibody; its specificity is assumed to be due to the occurrence of common or related proteins in the various strains of spirochaetes.

It is concluded that the RPCF is a simple and reliable test for the diagnosis of the treponematoses.

*T. E. Osmond*

KIRÁLY, K. Der Wert der ohne Vorbehandlung des Serums durchgeführten Treponema pall.-Agglutination für die Bestätigung des positiven Ausfalls der Lues-Reaktion. [**The Significance of *Treponema pallidum* Agglutination performed without Pretreatment of the Serum, for the Confirmation of the Positivity of the Lues-Reaction**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Apr., v. 117, No. 4, 317–24. [15 refs.]

Very full details are given of the method of preparing the spirochaete suspension from the rabbit testicle and also of the method of exhausting the reagin present in sera.

68 sera which had given positive results (mostly false) by the classical Kolmer, Kahn or Meinicke reactions, were subject to the treponema immobilization (TPI) test and treponema agglutination (TA).

The treponema agglutination test failed with a number of the TPI-positive sera and sera, positive by the TA test, were no longer so after absorption of reagin although they still gave a positive TPI test.

The conclusion is drawn that the TA test is not a good confirmatory test in VD laboratory work.

*J. W. McLeod*

CROOKES, Eileen M. L. & STUART, R. D. **The Value of Aerosporin in the Isolation of *Neisseria* from Swabs forwarded to the Laboratory in Transport Medium.** *J. Path. & Bact.* 1959, July, v. 78, No. 1, 283–8.

The detection of gonococci in smears from female patients is often time-consuming and difficult; cultures are often unsatisfactory owing to overgrowth of coliform bacilli. A search for some substance which would inhibited these but permit the growth of gonococci resulted in the discovery of aerosporin (polymyxin B sulphate).

At first various concentrations of this were incorporated in the transport medium used for swabs on their way to the laboratory but owing to the variations in time elapsing between the taking of swabs and their arrival in the laboratory this proved unsatisfactory, and incorporation in the final culture medium was tried.

Aerosporin 100, 50, 25 and 10 units per ml. was added to the medium and selected specimens containing coliform bacilli inoculated on to it. Coliform bacilli were inhibited in all concentrations and 10 units per ml. had no effect on gonococci.

Figures are given to show that this technique was highly successful and that the percentage of positive cultures of gonococci rose steadily after its introduction. It was therefore found possible to eliminate the examination of smears and rely solely on cultures in the case of patients who were under adequate control.

*T. E. Osmond*

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## GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

### GENERAL

ROGERS, D. E. **The Changing Pattern of Life-Threatening Microbial Disease.** *New England J. of Med.* 1959, Oct. 1, v. 261, No. 14, 677–83, 1 fig. [10 refs.]

"The hope that antimicrobial drugs would abolish infections as a cause of death has not been adequately realized." There appear, however, to have been changes in the types of infection that produce serious problems in hospital patients to-day. Specific information on this problem is lacking. In the present paper there is an analysis of "the incidence and nature of infections contributing to deaths on the medical service of the New York Hospital, contrasting the period 1957–1958 with the period 1938–1940". The study, the advantages and weaknesses of which are described, consisted of a detailed analysis of clinical records, laboratory data and autopsy protocols of 200 consecutive medical-service patients in each of the 2 periods. The results of the investigation are fully described with tables which set out bacteriological data, the number of primarily exogenous or endogenous infections, the incidence of serious underlying disease in patients dying primarily of infection and the place where infection was acquired whether outside or inside the hospital.

In 1938–1940 infections caused the death of 57 (28·5%) and infections of lesser significance were present in 51 (25·5%) of the 200 patients whereas in 1957–1958, 28 (14%) patients died as a direct result of microbial infections and in 30 others less critical infections

were present. The majority of fatal infections in the pre-antimicrobial period were caused by pneumococci, streptococci, tubercle bacilli and staphylococci but in 1957–1958 were commonly produced by Gram-negative bacilli, staphylococci, viruses and fungi. Fatal staphylococcal infections were not more common in the post-antimicrobial period. In the earlier period fatal infections commonly arose outside the hospital but in the later period 1957–1958 occurred most frequently within the hospital in patients already compromised by other serious diseases. *M. E. Delafield*

HOLT, L. B., BARNES, Joan M., BOUSFIELD, G., SPILLER, Violet & CROARKE, F. **A Comparison of the Antigenicity Characteristics of Mixed Antigens in the Child and the Guinea-Pig.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1121–32, 5 figs.

The respective responses of infants and guineapigs to mixed prophylactics containing diphtheria and tetanus toxoids and *Haemophilus pertussis* suspension are described and discussed. These were found to differ too widely to permit of a satisfactory evaluation of the probable antigenic response in the infant from the performance of the prophylactic in the laboratory. Since it is clear, however, that the addition of the vaccine does not diminish the child's response to the toxoids, and since the value of the incorporated toxoid has been established separately by animal test, it is suggested that any additional response due to the associated bacterial suspension may be accepted as a bonus without attempting to assess its exact value.

*J. W. McLeod*

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## HOSPITAL AND OTHER CROSS INFECTIONS

ANDERSON, A. **A Trial of Hexylresorcinol as Air Disinfectant in Day Nurseries.** *Med. Officer.* 1959, Oct. 23, v. 102, No. 17, 205–7, 2 figs.

"Hexylresorcinol was vaporised by electrical heat in the rooms occupied by the children in a group of day nurseries. For control purposes dummy vaporisers were used, changes made at 10 week intervals and the trial lasted 140 weeks. Records were kept of all absences of children and the reason given for such absences. A method was adopted in an attempt to assess the incidence of running noses among the children.

"The vaporisation of hexylresorcinol had no detectable effect on the incidence of running noses, on the days of absence due to respiratory tract infection or on the spread of infectious disease in the nurseries."

FORSGREN, U. & VARENIUS, P. Nosokomiala proteusinfektioner. [**Hospital** *Proteus Infections*] *Opuscula Med.* Stockholm. 1959, May, v. 4, No. 5, 189–95, 2 figs. English summary.

A comparison has been made of the incidence of hospital urinary infections in hospital patients in Stockholm due to *Proteus* in 1951–52 and in 1956–57. The results show that the incidence of *Proteus* has increased considerably, and has been accompanied by a fall in the proportion of infections due to *Escherichia coli* and other organisms. The number of strains of *Proteus* sensitive to sulphonamides declined from 32% to 14%, and to streptomycin from 82% to 12%, between the 2 periods, whereas sensitivity to chloramphenicol was retained. 71% of strains isolated in 1958 were sensitive to furadantin. *D. J. Bauer*

BROWNE, A. F., RYAN, E. A., GLASSOW, F. J., MARTIN, Caroline J. & SHOULDICE, E. E. **Staphylococcic Wound Infections. Study of Wound Infections in Several Thousand Hernia Cases.** *J. Amer. Med. Ass.* 1959, July 11, v. 170, No. 11, 1274–83. [13 refs.]

This long paper describes investigations of wound infection in 2 small hospitals performing only hernia operations; the study was prompted by evidence of an increased rate early in 1954 [though details of the rate are nowhere adequately presented]. Various investigations of skin disinfectants, glove puncture rates, and staphylococcal nasal carrier rates were uninformative until it was discovered that 1 of 4 surgeons had a post-operative sepsis rate of 7·3% while the others had rates between 1·0 and 1·9% [2 of these surgeons had, however, rates of 4·4 and 5·0% on operations at hospital B where most of the first surgeon's operations were performed]. The surgeon with the highest rate was a nasal carrier of type 81 staphylococci which were also the cause of the sepsis; he has subsequently worn a special face mask and he has had an infection rate of 1·4% [though it is not stated whether he continued to be a nasal carrier during this period]. Further laboratory tests showed that rather few staphylococci are in fact disseminated during nose breathing. It is recommended that special measures to protect against nasal carriers need only be taken after a carrier has been shown to harbour a dangerous strain.

The possible importance of airborne infection in the operating theatres was indicated by the fact that, of 91 operations during which air sampling revealed the presence of staphylococci, 9 (10%) were followed by infection, compared with 10 (4%) of 255 operations during which no staphylococci could be found.

*R. E. O. Williams*

BRADÁC, O., BROZ, O. & POLÁKOVÁ, H. Stafylokoková infekce a její podíl na kojenecké úmrtnosti v Libereckém kraji v letech 1953–1957. **[Staphylococcal Infections and their Rôle in the Mortality Rate in Liberec County in 1953–1957]** *Časopis Lékařů Českých.* Prague. 1959, May 29, v. 98, No. 22, 681–7. English summary.

An investigation has been made of the causes of death among 1,224 newborn infants dying between 1953 and 1957 in the Liberec district of Czechoslovakia. 400 deaths (32·67%) were due to birth injury, 253 (20·66%) to respiratory disease, and 178 (14·54%) to congenital malformation. 107 deaths (8·74%) were due to staphylococcal infection, and were analysed in further detail. Staphylococcal pneumonia was the cause of death in

69 (64·4%), skin infections in 28 (26·1%) and other forms of staphylococcal infection in 10 (9·3%) instances. The majority of deaths from staphylococcal infections over the 5-year period occurred between February and June, and infants aged up to 4 months were mainly concerned.

"In the last 2 years all births have taken place in the clinic, which is also the most frequent source of infection. A history of staphylococcal contact, either on the ward or in the family, could be found in 38 cases." *D. J. Bauer*

TEODOROVICI, G., BERNESCU, E., GHEORGHIU. M., CONSTANTINESCU, V., ZINGHER, S., GURĂNDEANU, B. & FORMAGIU, V. Unele considerații asupra contaminării cu stafilococ patogen într-un spital de pediatrie. [**Some Considerations on Contamination with Pathogenic Staphylococci in a Paediatric Hospital.** *Microbiol., Parazitol., Epidemiol.* Bucharest. 1959, July–Aug., v. 4, No. 4, 303–9, 1 fig. [17 refs.]

The English summary appended to the paper is as follows:—

"The authors comment on contamination with pathogenic staphylococci in a hospital of paediatrics. Pathogenic staphylococci were found in the nasopharynx and the faeces of the patients in a proportion of 35.7 per cent upon their admittance, and in 46 per cent of the cases upon their discharge. Sixty-one per cent of the hospital staff were found to carry the germs in their nasopharynx.

"The distribution of bacteriophage types in the isolated strains was varied, types of group III displaying the highest incidence-rate, in children as well as in the hospital staff. The incidence-rate of this type had increased at the children's discharge from hospital. Out of the children from whom pathogenic staphylococci have been isolated upon discharge, 75 per cent had been either negative at their admittance, or when positive, had carried different types. Most of the children had been kept in hospital for at least a week.

"The percentage-rate of antibiotic-resistance strains isolated upon discharge from the hospital displayed an obvious increase as compared to the percentage-rate found upon admittance."

COPPO, Anna & MAGLIOCCO, Fiora. Studio dei portatori di *Micrococcus pyogenes* tra i pazienti di una clinica chirurgica. [**Carriers of** *Staphylococcus aureus* **in Surgical Wards**] *Nuovi Ann. d'Igiene e Microbiol.* 1959, May–June, v. 10, No. 3, 191–200. English summary.

Nasal and anal swabs were taken from 110 patients of both sexes in the surgical wards of the University of Rome. The aim was to ascertain the percentage of carriers, any possible relationship between the presence of the organism in the upper respiratory passages and the anal and perianal regions, whether the organisms were all of one phage type, their resistance to antibiotics, and possible relation between the type of organism and the date of admission of the patient in the ward.

Swabs were plated on Chapman's medium, all non-haemolytic organisms were excluded, and the coagulase, gelatin, and antibiotic resistance tests were carried out in the usual manner. It was found that 53 nasal and 22 anal swabs were positive; in 12 patients swabs from both areas were positive, 7 of these strains were identical, 5 were different. The majority of the strains belonged to types I and III; 23 were untypable. 21·3% were coagulase negative. 10 strains were sensitive to all antibiotics (penicillin, streptomycin, tetracycline, chloramphenicol and novobiocin) 10 resistant to penicillin only, 11 to novobiocin only, and no less than 25 semi-resistant to chloramphenicol. Of the untypable strains only 2 were sensitive to all antibiotics, 3 resistant to penicillin only. 16 coagulase-negative strains were isolated, none was typable. Organisms belonging to type I were resistant to penicillin only, those in type III to streptomycin and tetracycline also. The authors point out that compared with a previous investigation on nurses, the percentage positive is rather low. This is considered to be due to the fact that the patients were all in the 40–50 age group while the nurses were much younger, and it is known that in children the percentage is very high. No relationship between date of admission and the presence of staphylococci was found. *W. K. Dunscombe*

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## COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neissera, Others.*

GOSLINGS, W. R. O., MULDER, J., DJAJADININGRAT, J. & MASUREL, N. **Staphylococcal Pneumonia in Influenza in relation to Antecedent Staphylococca. Skin Infection.** Lancet. 1959, Sept. 26, 428–30.

Many articles have been published on staphylococcal pneumonia complicating the epidemic influenza of 1957–58, but this, from Leiden, is the first encountered by the abstracter in which a correlation between staphylococcal skin lesions, present in the patient or his family, and staphylococcal pneumonia has been investigated. The correlation turns out to be quite high. Among 40 patients with staphylococcal-influenza pneumonia investigated, an identical strain of staphylococcus was isolated in 14 (35%) from the skin lesion and from sputum or pulmonary material, and in a further 8 cases (20%) the correlation appeared probable according to the facts available. In only 2 cases (5%) was a definite negative correlation found. A proven or probable correlation was also found in another 32 cases from various hospitals in Holland.

It is therefore recommended that a patient with influenza who has also a staphylococcal skin lesion himself, or in his family or other close contact, should be carefully watched and treated from the beginning of a pulmonary complication, or even prophylactically with the right antibiotic.

As in many other reports, the staphylococci isolated from patients a few days after admission to hospital

were often found to differ from those present on admission, and were more antibiotic-resistant.

*H. Stanley Banks*

BRUMFITT, W., O'GRADY, F. & SLATER, J. D. H. **Benign Streptococcal Sore Throat.** *Lancet.* 1959, Sept. 26, 419–23. [39 refs.]

This is an important article which carries a step further the elusive distinctions between streptococcal and non-streptococcal sore throat, and between the sore throats from which streptococci are isolated when there is and when there is not evidence of streptococcal invasion of the body.

The problem was first studied by assessing the spread of group A streptococci found in the throats of healthy recruits to the community in which they lived. Only a slight increase in the carrier-rate was found and this was not associated with the appearance of sore throats. Next, a study was made of 242 patients admitted to hospital with acute febrile sore throat. Group A streptococci were isolated from 57–88% of these patients, and the streptococcal and non-streptococcal cases were indistinguishable clinically (as has been found by others). Only 16% of the patients with streptococci showed a significant rise in anti-streptolysin O titre, and no first attacks of rheumatic fever were seen. It seemed therefore that evidence of streptococcal *invasion* was present only in a relatively small proportion of the cases of proved streptococcal sore throat.

It was concluded that mere isolation of Group A streptococci from acute sore throats was insufficient proof that streptococci were the primary cause of the illness; the illness might well be viral in origin with the streptococcus playing a mere opportunist role. Most of the patients in this series with so-called streptococcal sore throat seemed to fall into this category, and a new name is proposed for this condition—benign streptococcal sore throat. Such cases do not require penicillin treatment, which should be reserved for those who have had rheumatic fever in the past, and for epidemics in which the streptococcal isolation rate approaches 100%, in which case the organisms may be assumed to be of enhanced virulence. When penicillin is given it should be adequate to eliminate the streptococci—a course of 7 days at least. *H. Stanley Banks*

SASLAW, M. S., JENKS, Sallie A. & SAUL, Madelyn. **Frequency of Recovery of Beta Hemolytic Streptococci as related to Number of Throat Swabs.** *J. Lab. & Clin. Med.* 1959, July, v. 54, No. 1, 151–4.

Throat cultures were taken in quadruplicate from 274 persons, in most cases in 2 successive swabbings with "double" swabs. 1 of each pair of swabs was plated on each of 2 blood agar media. 58 persons yielded haemolytic streptococci, 31 being Group A. In only 12 were all 4 cultures positive and in 24 the streptococci were isolated from only 1 of the 4 cultures. 18 of the 24 had 10 or fewer colonies on the single positive plate, compared with 17 of the 48 plates from the former. [*Cf.* COMMISSION ON ACUTE RESPIRATORY DISEASES, this *Bulletin*, 1950, v. 25, 308.]

*R. E. O. Williams*

MAINARDI REYNA, L. Estudio retrospectivo de un brote de fiebre escarlatina en 1958, en Ponce, Puerto Rico. [**Retrospective Study of an Outbreak of Scarlet Fever in Ponce, Puerto Rico, in 1958**] *Bol. Asoc. Med. de Puerto Rico.* 1959, July, v. 51, No. 7, 243–57, 4 figs. [47 refs.]

Scarlet fever was not prevalent in Puerto Rico until it began to be imported from the USA. The outbreak now reported began in January 1958 and during that year 343 cases came to official notice in the whole island, of which 275 were in Ponce, an industrial town, of 145,900 inhabitants, of whom 59,682 are under 15 years of age. This is the first recorded outbreak in the island though streptococcal carditis is not uncommon and in one town there was once a series of cases of glomerulonephritis thought to be due to a streptococcal infection.

The clinical signs in the Ponce epidemic are described and are typical of classical scarlet fever.

Except for some in Group C the organism isolated was a beta-haemolytic streptococcus of Lancefield Group A mainly of the Griffith types 1, 2, 3, 4, 5 and 11. The complicated cases showed types 2 and 11.

Transmission was presumably by droplet infection though it is suggested that the first wave was due to something "probably alimentary". Milk was, however, excluded.

Only 4% of the contacts developed the clinical disease but many contacts gave an immune reaction and probably had a sub-clinical illness. There were 4 cases in January and 66, 61, 54 and 44 in the 4 following months: after July the incidence rapidly declined. For the year the incidence was 188·4 per 100,000 inhabitants; in the adjoining town of Adjuntas it was 153·5 but the rest of the island was relatively free. In Ponce the age-group most affected was 5–9 years with an incidence of 570·2 per 100,000 of those ages: it was 516·9 at ages 10–14 and 200·5 for those under 4 years.

Only complicated cases were admitted to hospital: there were 4 patients with nephritis and 2 with rheumatic fever.

In 1959 throat swabs were examined from 98 children in a school where there had been 4 cases of scarlet fever in the previous year: a haemolytic streptococcus was grown in 43. In 1958 the children in 2 other schools were Dick-tested and between 30 and 45% of those aged 6 to 10 gave positive results.

The routine treatment was penicillin for at least 10 days. Complications are apt to occur if treatment is discontinued as soon as the symptoms subside. Contacts can be protected by a 5–10-day course of antibiotics or sulphonamides.

Control was effected by isolation of the patients at home or in hospital and exclusion from school or work until throat swabs were free from haemolytic streptococci: there is no need to close schools or places of work: contacts should be protected on the lines

mentioned above: current disinfection of clothing, table utensils and toys is advisable but terminal disinfection is of doubtful value: looking for carriers at school or factory is hardly worth while. *Allen Daley*

JULKUNEN, H. & KAIPAINEN, W. J. **Rheumatic Fever and Antistreptolysin-O Titre.** *Ann. Med. Intern. Fenniae.* Helsinki. 1959, v. 48, No. 2, 81–5.

Taking a titre of 200 as the upper limit of normal, the authors found a raised antistreptolysin-O in only 47% of 106 patients treated for rheumatic fever between 1949 and 1958 in the second medical clinic of the University of Helsinki. Previous series quoted had reported raised titres in 76–95%. The patients with a raised titre showed more rheumatic symptoms but a low titre did not exclude carditis. *A. B. Christie*

LENDRUM, Bessie L., SIMON, A. J. & MACK, I. **Relation of Duration of Bed Rest in Acute Rheumatic Fever to Heart Disease present 2 to 14 Years Later.** *Pediatrics.* Springfield, Ill. 1959, Sept., v. 24, No. 3, 389–94.

This is an attempt to compare in 2 groups of patients suffering from rheumatic fever the effect on subsequent cardiac status of short or prolonged bed-rest. 269 patients were allowed graded activity as soon as acute symptoms and signs subsided: 91 were given prolonged bed-rest. Other factors such as quality of medical care, prophylactic medication and rheumatic recurrences were taken into account in assessing results and the authors conclude that prolonged bed-rest and restriction of activity after an attack of acute rheumatic fever is not necessary and may be a disadvantage.
*A. B. Christie*

TIDWELL, R. A. & LEWIS, D. **Erythromycin Prophylaxis. A Four Year Study.** *Antibiotic Med.* New York. 1959, July, v. 6, No. 7, 395–400.

This study was designed to ascertain the efficiency of erythromycin in the prophylaxis of group A β-haemolytic streptococcal disease [presumably as a substitute for penicillin]. Children aged 3 months to 15 years were given, irrespective of age, 100 mgm. in a tablet or 125 mgm. in fluid form once daily for 4 years. At first monthly blood counts, throat cultures, urine analysis, and stool cultures were done, but after the first year throat cultures only were done, as no changes were noted in the other tests. Cultures were also obtained at frequent intervals from the families of each patient.

The results showed a definite *decrease* over the years of staphylococci and of Group A β-haemolytic streptococci in the throat cultures of the patients. The family patterns were not changed. It is concluded: (1) that erythromycin can be substituted for penicillin in prophylaxis, (2) that prolonged and continuous use of erythromycin is not deleterious, nor does it lead to the appearance of erythromycin-resistant coagulase positive staphylococci, and (3) that the staphylococcal pattern in the family group is not apparently affected by this prolonged use of erythromycin. *H. Stanley Banks*

WAITE, C. L. & KLINE, A. H. **Mima Polymorpha Meningitis. Report of a Case and Review of the Literature.** *J. Dis. Children.* Chicago. 1959, Sept., v. 98, No. 3, 379–84. [25 refs.]

*Mima polymorpha*, first isolated in 1939 from urethral discharge, has been reported as a rare cause of meningitis [this *Bulletin*, 1958, v. 33, 1110] and in this article a further case in a child of 6 years old is reported. Cerebrospinal fluid in this case was normal in appearance, cell count and chemistry but the organism was isolated on culture and the authors cite other cases where the cerebrospinal fluid was little altered from normal [*ibid.*, 1958, v. 33, 705]. Clinically the illness may resemble both meningococcal and aseptic meningitis. The organism appears to be most often sensitive to oxytetracycline although this drug has apparently never been used in treatment: in the case reported, recovery followed the use of sulphadiazine and chloramphenicol. *A. B. Christie*

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## BACTERIAL INFECTIONS

The order is:—*General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.*

PARIKH, M. M. & THANAWALA, J. K. **Diphtheria. A Study of Clinical Features with relation to Bacteriological Types of *C. diphtheriae*.** *Indian J. Child Health.* 1959, Oct., v. 8, No. 10, 511–22.

This is an attempt to correlate clinical severity with cultural type of organism in 127 cases of diphtheria. Fever, increased salivation, vomiting and refusal of feeds were commoner in the *gravis* group, pain in the throat, cough, swelling of the neck, hoarseness and pain in the ears in the *mitis* group. [In the table illustrating these findings, the figures seem to be the wrong way round, those from *gravis* types appearing under *mitis* and *vice versa*.] 101 of the organisms were *mitis*, 23 *gravis* and 3 *intermedius*. *A. B. Christie*

AGARWAL, S. C. & HOLT, L. B. **Local Factors in the Pathogenesis of Circulatory Failure in Diphtheria.** *J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 381–8, 5 figs. (4 on pl.).

The authors have sought evidence with regard to the mechanism of vasodilatation under the influence of diphtheria toxin. For this purpose they have studied the effect of various drugs on the area of vasodilatation, by positive Schick reaction, in the guineapig skin and also on the iris of rabbits injected with toxin to the outer chamber of the eye, and in control animals.

Both types of experiment indicated a diminished sensitivity of the sympathetic nerve endings in the involuntary muscles to adrenaline and noradrenaline as the cause of the capillary dilatation and it is suggested that such dilatation of the finer blood vessels may be an important contributory factor to circulatory failure in diphtheria. *J. W. McLeod*

BERG, J. M. **Neurological Sequelae of Pertussis with particular reference to Mental Defect.** *Arch. Dis. in Childhood.* 1959, Aug., v. 34, No. 176, 322–4. [13 refs.]

A child of 10 months suffering from whooping cough developed severe apnoeic attacks followed by a state of semi-coma with hypertonicity of limbs. After recovery from the acute illness, the child's physical development was normal but her mental state at 3½ years old was that of an imbecile. The author briefly reviews some of the literature [this *Bulletin*, 1943, v. 18, 358; 1951, v. 26, 201] and tentatively considers the mental condition as being due to cerebral anoxia during the apnoeic attacks.

*A. B. Christie*

DENIE, J. J. P. A. Letale colitis door *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*), na antibiotische behandeling van een patiënt met sepsis door *Streptococcus viridans*. [**Fatal Colitis due to** *Pseudomonas pyocyanea* **following Antibiotic Treatment of Sepsis caused by** *Streptococcus viridans*] *Nederl. Tijdschr. v. Geneesk.* 1959, Nov. 7, v. 103, No. 45, 2263–6, 4 figs.

The English summary appended to the paper is as follows:—

"A woman, aged 61, was treated with antibiotics for sepsis due to a *Streptococcus viridans* infection. She developed a condition resembling staphylococcous enteritis, which was caused by colitis due to *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*)."

TIGANO, F. & LA ROSA, F. Il quadro emocoagulativo nella infezione tifoide. [**Blood Coagulation Changes in Typhoid**] *Giorn. di Malattie Infettive e Parassit.* 1959, Aug., v. 11, No. 8, 691–704, 4 figs. [138 refs.]

The following is a translation of the authors' summary:—

In a study of coagulation and haemostasis tests in 38 typhoid patients the authors found, in about half the patients, a decrease in the amount of prothrombin and of factor VII (55% to 79% fall in activity) and in about 20% a reduction in the maximum width of the thrombo-elastogram (40–45 mm.). Coagulation time, Howell's recalcification time, the test for heparin tolerance *in vitro* and the fibrinogen estimation gave generally normal figures; the number of blood platelets was reduced but never below 100,000; a defective contraction of the coagulum was present in those patients with a reduced *ma* curve; *r* and *k* values in the thrombo-elastogram tracing were within normal limits though tending towards the higher limits.

The authors are inclined to attribute the fall of the prothrombin complex to functional liver changes of a toxic origin, and the reduction in the *ma* curve to functional platelet deficiency which was associated with the toxic state; they point out that combined treatment with chloramphenicol and prednisone was effective in restoring blood coagulative characters to normal.

Throughout the article the literature on the subject, including that on the aetiological aspect, is referred to and fully summarized. The authors give considerable importance, when dealing with melaena and other haemorrhagic manifestations of typhoid, to allergic factors.

*E. Agius*

NETER, E., DRISLANE, Anne M., HARRIS, A. H. & GORZYNSKI, E. A. **Study on Antibodies against Enteric Pathogens in Human Gamma Globulin.** *Amer. J. Pub. Health.* 1959, Aug., v. 49, No. 8, 1050–59. [29 refs.]

The term "enteric pathogens" here implies any Gram-negative bacillus found in the human intestine that is considered to be pathogenic. Antigens prepared from cultures of such organisms were used in the haemagglutination test and compared with the conventional bacterial agglutination test for the detection of complete antibodies in human gamma globulin from various sources against the various antigens. The antiglobulin haemagglutination test and an enzyme haemagglutination test were used for the detection of incomplete antibodies. The latter test involved the use of a number of different enzymes—trypsin, chymotrypsin, protease, papain etc.—which were added to the red blood cells sensitized with the various antigens. After washing, the cells were then put up against the gamma globulin.

The Coombs test was considered positive if the addition of anti-human globulin to the sensitized red cells, that had failed to show a positive haemagglutination test, now gave agglutination or if the anti-human globulin produced enhanced agglutination.

The commercial gamma globulin preparations were obtained from a number of sources which included U.S.A., U.K., India, Japan and Australia. In most cases the antibody levels against the various antigens did not differ significantly whatever the source of the gamma globulin. There were, however, two striking exceptions. Complete antibodies against Shiga's dysentery bacillus were very low in gamma globulin from U.S.A. and Japan and against paratyphoid A in preparations from U.S.A., U.K. and Japan while in gamma globulin from India the levels of both these antibodies were reasonably high. The interest of these results lies in the fact that paratyphoid A is a very uncommon disease in U.S.A. and U.K. whereas it is endemic in India, in many parts of which it is the commonest of all the enteric group of fevers. This picture has not changed over the years. Shiga dysentery has steadily become less common all over the world in recent years but it was frequently seen in the East, including India, and still occurs in some areas there, but the only cases seen in the United States and Great Britain at the present time are in the very few patients who contracted it in Eastern theatres.

Whatever may be the protective value of gamma globulin in infections caused by the organisms investigated (this is discussed by the authors), the specificity of the haemagglutination test, which was checked by absorption procedures in the work reported, receives support from the epidemiological data and the geographical distribution of some of the infections considered.

*H. J. Bensted*

PARNAS, J. Recherches concernant l'allergie et les allergènes au cours de la brucellose. [**Investigations with regard to Allergy and the Substances which provoke it in Brucellosis**] *Rev. d'Immunologie.* 1959, Jan.–Mar., v. 23, Nos. 1/2, 74–96. [23 refs.]

This is a summary of results of many years of work on the preparations of brucellae used in the production of allergic reactions for diagnostic purposes. Results of a variety of skin tests are compared with one another and with the humoral phenomena of immunity depending on agglutinating and complement-fixing antibodies. The superiority of the allergic reactions to the other immunity phenomena in this condition already claimed [see this *Bulletin*, 1959, v. 34, 334, 439] is further emphasized.

The results of observations on patients with the disease and experimental observations on the rabbit are set out in many extensive tables and a very large number of preparations from brucella cultures coming from many parts of the world have been compared. For allergic skin reactions in brucella infections, BURNET'S technique was found to be best and to be particularly reliable in chronic cases. Of the many preparations tested, Brucellin PD, which is officially recommended by the Polish Ministry of Health, has been found to be the best. Particulars are also given of the results which have been obtained in the treatment of persisting human infection with PD and of the gradation and number of doses which should be given. The preparation PD ("*ad usum therapeuticum humanum*") is described as follows: it is prepared from a mixed suspension of specially chosen strains of high antigenic activity which have come from different parts of the world. These are listed. The suspension is broken up by exposure to ultrasonic vibrations at 2,800 kilocycles/second and killed by exposure to a temperature of 58–60°C. for 30 minutes.

The preparation, which corresponds to a concentration of 5,000 million cells/ml. is diluted before use according to the stage of immunization which has been reached by the patient. *J. W. McLeod*

CONDREA, P., PENCEA, I., RANTA, V., GHILEZAN, I., MURESAN, T., KUN, M., SASU, A., SAVA, V. & MARKES, G. Épidémie de tularémie de type professionnel déterminée par le *Cricetus cricetus*. [**Occupational Tularaemia Epidemic caused by** *Cricetus cricetus*] *Arch. Roumaines Path. Expér et Microbiol.* 1959, June, v. 18, No. 2, 175–9, 4 figs.

The epidemic of tularaemia which is described here is called "professional" since it occurred as an occupational risk in that the cases of infection occurred only among fur hunters. The number of hunters who were infected was 44 or about 50% of those engaged. Of these cases of infection most occurred during the trapping season of January to June in 1955. All the hunters were occupied in catching the rodent *Cricetus cricetus* for its fur.

The disease which began usually in 2–7 days after 1 of these animals had been skinned by the hunter took various forms such as glandular enlargement in the upper extremities, visceral disturbance and pulmonary involvement. The infection was diagnosed clinically, by skin reactions to tularin and serologically. No ocular manifestations were observed and there were no deaths.

Prior to 1955 it had been considered that this rodent *Cricetus cricetus* played only a negligible role in causing tularaemia. During this epidemic it was observed that the animal had increased very greatly in numbers and also that it was suffering a heavy mortality.

*M. E. Delafield*

CLAUS, K. D., NEWHALL, J. H. & MEE, D. **Isolation of** *Pasteurella tularensis* **from Foals.** *J. Bacteriology.* 1959, Aug., v. 78, No. 2, 294–5.

Isolation of *Brucella tularensis* from equines does not seem to have been recorded hitherto. The present authors report its isolation from 2 foals and a rise in antibody titre in mares and foals suffering from a febrile illness. The animals were on a pasture in a rough grazing area in Montana where tularaemia is endemic in small ground game: the area is heavily infested with ticks.

A mare and 5 foals developed an acute fever, lasting about a week, with symptoms which included stiffness, oedema of the limbs, dyspnoea and incoordination. All animals except 2 of the foals recovered after antibiotic treatment; the mare's serum showed an agglutination titre of 1 in 160 against *Br. tularensis* three weeks later. The 2 foals which did not survive died at the age of 10 and 14 days. Autopsy showed swelling and small necroses in the liver, spleen and kidneys and epicardial petechiae: in one foal there was lobular consolidation in the lungs. An organism indistinguishable morphologically and biochemically from *Br. tularensis* was isolated in pure culture from all these organs, except the heart: it was highly pathogenic for guineapigs.

The surviving animals showed rising antibody titres up to 1 in 640 with the isolated culture and with *Br. tularensis*. High titres were also found in one apparently unaffected mare. The serum of this animal and of an affected foal fell to low levels in 14 and 25 days respectively and 5 months later the sera of all the horses were negative, except 1 which showed a titre of 1 in 20. This rapid disappearance of agglutinin is contrasted with the persistent titres found in sheep and man.

The serological results in apparently healthy horses suggest that they had a transient sub-clinical infection: the significance of this was heightened by the finding of antibodies against *Br. tularensis* in 2 horses which were infested with ticks and were in contact with a flock of sheep infected with tularaemia.

*H. J. O'D. Burke-Gaffney*

CHARKES, N. D. **Hemagglutination Test in Tularemia. Results in 56 Vaccinated Persons with Laboratory Acquired Infection.** *J. Immunology.* 1959, Aug., v. 83, No. 2, 213–20, 6 figs. [18 refs.]

"Agglutinin and hemagglutinin titers were determined in 59 cases of laboratory-acquired tularemia occurring in 56 vaccinated persons. A 4-fold rise in agglutinins was observed, on the average, on the 19th day of illness and the mean peak titer of 1:1280 sometime during the second or third month. Thereafter,

agglutinins fell slowly and were detectable as long as 12 years after infection, closely paralleling the response seen in naturally-occurring tularemia.

"Hemagglutinins reached diagnostic levels on the 11th day, on the average, and the mean peak titer of 1:10,240 occurred during the second month. Hemagglutinins also persisted in the serum for years, at somewhat higher levels than agglutinins.

"By the end of the second week of illness, 38% of patients had 4-fold or greater increases in hemagglutinin titer, but only 15% had had a diagnostic rise in agglutinins.

"In 26 cases, sera were collected frequently during the acute phase of illness. In 14, a diagnostic level of hemagglutinins occurred earlier, and in the other 12 4-fold increases of both antibodies occurred at the same time. In no case did agglutinins rise earlier.

"In eight patients there was no change in antibody titer during the course of illness. This was possibly due to prior elevation from booster vaccination within 6 weeks of onset of disease, or reinfection (proved or probable). In one case there was a rise in hemagglutinins although agglutinins did not change."

SEMPLE, A. B. & HOBDAY, T. L. **Control of Anthrax. Suggestions based on Survey of Imported Hides.** *Lancet.* 1959, Oct. 3, 507–8.

Although a large tonnage of hides is imported through the port of Liverpool chiefly from Argentina, East Africa and West Africa—countries in which anthrax is enzootic with epizootic incidents—the disease is rare in Liverpool docks where only 7 cases were reported in the period 1954–58.

In order to assess the danger 1,053 separate samples from hides were taken in 1958 immediately after discharge from ships. The method of sampling, subsequent treatment of samples and testing of these by inoculation of material into guineapigs are described. The results of the investigation are set out in a table. It was found to be likely that at least 1 hide in 4 is contaminated with anthrax organisms. The range of positives for anthrax was from 3·1% in Argentine cattle to 48% in West African sheep. Commercial grading of the hides for quality was found to be unrelated to incidence of anthrax infection.

Since this incidence is so high and yet anthrax is very rare in those who handle hides, it is suggested that the natural human resistance to anthrax must be greater than is generally supposed. "For further protection against the disease, reliance should perhaps be placed on immunising procedures rather than on the extension of physical precautions." *M. E. Delafield*

SCHMID, A. W. Estudos sôbre a mortalidade por várias causas no Município de São Paulo. II. Tétano. [**Studies on the Mortality by Several Causes in the Municipality of Sao Paulo. II. Tetanus**] *Rev. Inst. Med. Trop. São Paulo.* 1959, July–Aug., v. 1, No. 2, 89–98, 4 figs. [10 refs.] English summary.

In 6 out of 11 towns in Brazil where the statistics were examined the death rate from tetanus increased between 1942 and 1951. In São Paulo in 1953–57 there were 592 deaths from tetanus out of 136,087 from all causes: this is 0·44% and compares with 0·31% in 1898–1902 and 0·19% in 1918–20. A table gives the tetanus death rate per 100,000 population in São Paulo year by year from 1894 when it was 11·12 to 1957 when it was 3·77. In recent years the rate has been relatively unchanged and has not shown the decline that most of the other communicable diseases have done. In São Paulo the male death rate from tetanus during 1948–57 was 5·40 per 100,000 population and the female 3·07. The vast majority of the deaths, 63·93%, were at ages under 1 year and of these 91·25% occurred during the first 14 days of life. There were 596 deaths from tetanus of children under 1 year in São Paulo in 1950–57: 153 were on the 7th day of life and 233 during the second week. There was no marked variation in the seasonal incidence.

The conclusion is that umbilical tetanus is a serious public health problem in Brazil. Suggested preventive measures are: (1) instruction on the nature, cause and dangers of the disease to be given to expectant mothers and those, generally untrained, who attend the births; (2) an increase in the number of trained midwives and public health nurses; and (3) vaccination against tetanus of pregnant women. *Allen Daley*

WRIGHT, W. B. **Management of Tetanus with Oral Chlorpromazine.** *J. Roy. Nav. Med. Serv.* 1959, v. 45, No. 2, 99–103, 2 figs.

A 4-year-old boy suffering from tetanus was sedated with chlorpromazine 200 mgm. daily in 3-hour doses and chloral hydrate 40 grains daily in 6-hour doses, both by mouth. Chlorpromazine was continued for 18 days and chloral hydrate for 12 days. Spasms were fully controlled and the boy made an excellent recovery.

*A. B. Christie*

COHEN, H., VON RAMSHORST, J. D. & TASMAN, A. **Consistency in Potency Assays of Tetanus Toxoid in Mice.** *Bull. World Health Organisation.* 1959, v. 20, No. 6, 1133–50, 2 figs. [23 refs.]

Experimental work on the immunization of mice with the fluid tetanus toxoid which has been used for guineapig tests and accepted as the International Standard are not sufficiently consistent for the development of a standard based on tests in mice.

The much lower cost and the greater facility in breeding makes it desirable to have a test which can be carried out with these animals. It has been found possible to do this if a tetanus toxoid adsorbed on aluminium phosphate is used in place of the fluid toxoid.

*J. W. McLeod*

MOCHMANN, H. & MAHNKE, P. F. Die Leptospirosen des Hausschweines und deren Bedeutung für die Epidemiologie menschlicher Leptospirenerkrankungen. [**Leptospirosis in Pigs and its Importance for the Epidemiology of Leptospiral Diseases in Man**] With an introduction by J. KATHE. *Beiträge z. Hyg. u. Epidemiol.* Leipzig. 1959, No. 13, 53 pp., 3 figs. [148 refs.]

The greater part of this small but comprehensive monograph is devoted to a review of the literature on

leptospirosis in pigs in different parts of the world. The 143 articles cited cover reports of work from 26 countries in all 5 continents, and easy reference is assured by the fact that each country is dealt with separately. The authors have included also a series of tables which set forth in detail the different serotypes found in these countries together with the criteria (where available) on which the results of serological tests were based. This is particularly useful because there is considerable divergence of opinion as to the interpretation of low positive agglutination titres in the sera of domestic animals. The reader is thus enabled to decide for himself what credence to attach to the reports.

Other sections deal briefly with the epidemiology, clinical aspects and therapy of leptospirosis in pigs. Though generally a mild or even symptomless infection in these animals, pigs are important carriers of *Leptospira pomona* which causes "swineherds' disease" in man and which in the U.S.A. is widespread among cattle [causing an estimated loss of about 100 million dollars a year mainly as the result of abortions and loss of milk yield].

The last section deals with the authors' own investigation of material from 1,000 pigs slaughtered in Rostock. Samples of serum were tested for the presence of agglutinins against a representative range of 16 serotypes of leptospires; cultures were made from liver and kidney; and sections of these organs were stained by silver impregnation for microscopical examination.

The cultural and microscopical investigations gave negative results for all the 1,000 pigs. Agglutination tests (taking a dilution of 1/400 as the significant level) were positive with 45 (4·5%): in detail *L. icterohaemorrhagiae*, 34; *L. andaman*, 6; *L. pomona*, 3; *L. bataviae*, 1; and *L. grippotyphosa*, 1. It appeared therefore that pigs are not important in the epidemiology of leptospirosis in the Rostock area.

This monograph should prove of great use to all who are interested in the problems related to leptospirosis in domestic animals. *J. C. Broom*

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## VIRUS INFECTIONS

The order in this section is:—*General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Enteric group; Arthropod-borne group; Others.*

BUŞILĂ, V. T., VASILESCU, I., FITĂRĂU, A. & MONTAG, I., in co-operation with D. SĂRĂTEANU, Elena OPRESCU-LISIEVICI & Elisabeta NASTAC. Contribuţii la clinica ornitozei. [**The Clinical Features of Ornithosis**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1959, Mar.–Apr., v. 4, No. 2, 133–43, 9 figs. [28 refs.]

An account is given of the clinical aspects of 19 serologically confirmed cases of ornithosis which occurred in Timisoara, Rumania, in 1957–58. The clinical course was mild in 6, moderate in 10 and severe with nervous involvement in 3 cases. A possible source of infection could be established in only 5 instances. In 4 cases the onset was insidious; the febrile period lasted for 7–11 days in the pseudo-influenzal form and for 5–15 days in the pneumonic form of the disease. The initial symptoms included rigors, fever, headache, myalgia, constipation, bradycardia, herpes labialis, dry cough with mucous sputum, dyspnoea and cyanosis. 5 case histories are given in illustration. *D. J. Bauer*

ALVSAKER, J. O. Ornithose méd miliaert lungebilde og uvanlig forløp. [**Ornithosis. A Case with Miliary Densities of Both Lung Fields and an Exceptional Course**] *Nordisk Med.* 1959, Oct. 22, v. 62, No. 43, 1550–52, 2 figs. [26 refs.]

The English summary appended to the paper is as follows:—

"A case of pulmonary ornithosis with symmetrical miliary densities of both lung fields and a rather protracted course complicated by changes in the heart contour and reduced vital capacity is reported.

"There was no evidence of primary heart involvement. Corticoid therapy produced striking improvement. According to the theory of a viral infection as an aetiological factor in diffuse interstitial fibrosis of the lungs (Hamman-Rich syndrome), it is suggested that our case might represent an intermediate stage between a benign viral infection and the syndrome of Hamman-Rich."

FREDERIKSEN, H., TORRES MUÑOZ, N. & JAUREGUI MOLINA, A. **Smallpox Eradication.** *Pub. Health Rep.* Wash. 1959, Sept., v. 74, No. 9, 771–8.

This paper describes a campaign to eradicate smallpox from Bolivia. The country is thinly populated with very limited means of communication over wide areas. Hitherto vaccination has been inefficient. Preparations for a nation-wide campaign were made in 1957 after the onset of an epidemic wave of smallpox centred on Cochabamba, the central department of Bolivia. The campaign was conducted by the *Servicio Cooperativo Interamericano de Salud Pública* under the auspices of the Ministry of Public Health of Bolivia and the International Co-operation Administration of the United States, and was based on methods first developed in Iran [FREDERIKSEN and SHEEHY, this *Bulletin*, 1958, v. 33, 97].

11 teams—a total of 83 persons—were provided with transport—4-wheel-drive vehicles equipped with winches and loudspeakers, while 3 river teams travelled by launch. Unrefrigerated lyophilized vaccine only was used. The vaccine was reconstituted in the field with a 50% solution of glycerin and distilled water: any of this remaining at the end of the day was discarded. A single scratch of about 5 mm., with a disposable pin, through a drop of vaccine on the untreated skin over the insertion of the left deltoid muscle was the standard technique used. At the same time the left little finger of the vaccinated person was dipped in indelible ink for future identification. No records were kept other than the number of vaccinations and the lot number of the vaccine. Inspectors followed the vaccinators, reading results on the ninth day in samples consisting of a sufficient number of households to obtain, if possible, a total of at least 100 people in each section covered by one vaccinator in one day. The inspector recorded

name, age, evidence of previous smallpox, and previous and current vaccination with type of take in each person in the samples. The public were informed of what was going on by all available means and co-operated well. Everyone was vaccinated regardless of age, sex, or previous history. Only those less than 4 weeks old, those acutely ill, and those with eczema were excepted. By the end of 1958 some 2,432,186 persons—about three-quarters of the estimated population of Bolivia—had been vaccinated. Inspection of primary vaccinations of 3,662 infants in widely distributed samples showed 96·3% primary takes. [No reference is made to any complications or ill effects.]

In 1957 Bolivia suffered the highest smallpox attack rate in the Americas. Since November 1958 no case has been reported. It is intended in 1959 to send 4 mobile teams to those sparsely populated and remote areas hitherto not reached.

The authors' thesis is that here is an example of how smallpox can be eradicated from an endemic area. If it were possible for similar methods to be applied to other endemic foci, especially in Asia and Africa, then smallpox could be banished from the world. [For global success to be achieved all such campaigns would need to be conducted more or less simultaneously.] Meanwhile, any country which has rid itself of smallpox remains at risk of re-importation of infection and of re-establishment of the disease. *J. Pickford Marsden*

DiMase, J. D., Groover, R. & Allen, J. E. **Artificial Respiration in the Therapy of Primary Varicella Pneumonia.** *New England J. of Med.* 1959, Sept. 10, v. 261, No. 11, 553–5, 2 figs. [14 refs.]

A man aged 29 developed haemorrhagic chickenpox with marked respiratory symptoms. He failed to respond to oxygen and intermittent positive pressure ventilation (presumably by a mask) and was eventually heavily sedated with morphia to depress voluntary respiration and successfully treated in a tank respirator. *A. B. Christie*

Heppleston, J. D., Pearce, K. M. & Yates, P. O. **Varicella Encephalitis.** *Arch. Dis. in Childhood.* 1959, Aug., v. 34, No. 176, 318–21, 5 figs.

A child aged 4 years and 9 months had a mild attack of chickenpox followed after 2 weeks by a fatal attack of encephalitis. At autopsy the striking feature was the localization of the inflammatory reaction to the grey matter of the cortex and basal nuclei. There was swelling of the endothelium of capillaries and venules with much surrounding microglial proliferation. Demyelination of the white matter was present in only a few areas of the brain but there was striking degeneration of the myelin sheaths of the spinocerebellar tracts in the upper part of the spinal cord.

The authors review the literature on the subject [this *Bulletin*, 1956, v. 31, 241] and conclude that the essential abnormality is damage to blood vessels, possibly of an allergic nature. *A. B. Christie*

Winkelmann, R. K. & Perry, H. O. **Herpes Zoster in Children.** *J. Amer. Med. Ass.* 1959, Oct. 17, v. 171, No. 7, 876–80, 3 figs. [12 refs.]

The authors record 7 cases of herpes zoster in children in 3 years and feel that the condition is commoner than is thought. Their youngest patient was 7 months old, the oldest 5 years. All the complications of adult zoster may occur in children except post-herpetic neuralgia. 2 of the patients had generalized herpes, one had local gangrene and one had meningeal symptoms with pleocytosis in the cerebrospinal fluid. Only 1 of the 7 patients had not had chickenpox before. *A. B. Christie*

Nikodémusz, S. Cercetări asupra imunității în parotidita epidemică. **[Investigations on Immunity in Epidemic Parotiditis]** *Microbiol., Parazitol., Epidemiol.* Bucharest. 1959, May–June, v. 4, No. 3, 211–17, 1 fig.

The English summary appended to the paper is as follows:—

"Serological investigations were carried out on epidemic parotiditis in patients, normal persons from an epidemic environment, and in vaccinated subjects. The serum of normal persons usually contains no S antibodies, while V antibodies can be detected to a dilution of 1/20. In epidemic environments, serological methods confirmed the existence of numerous silent infections. In patients, the first to become positive is the SCFR followed by the HAI test and finally by the VCFR on the 11th–14th day. Serological tests yielded positive results even in atypical cases of disease. In persons vaccinated by 2 inoculations with precipitated vaccine according to Koch's method, the HAI and VCFR tests demonstrated a high titre of antibodies which persisted for more than 100 days. The immunity obtained after a first inoculation of antigen S is only potential. Serological investigations show that precipitated vaccine conveys a lasting immunity."

Grist, N. R. **Asian Influenza in the Glasgow Area 1957–58.** *Scottish Med. J. Glasgow.* 1959, Sept., v. 4, No. 9, 446–50, 1 fig.

"Asian influenza first struck Glasgow in Autumn 1957." A major epidemic affecting all sections of the population ensued and there was an inconspicuous second wave of Asian influenza in the more usual winter season. This second wave was detected by laboratory investigations [this *Bulletin*, 1959, v. 34, 729]. Virus examinations, the materials and methods of which are described, were carried out on specimens from 649 patients in the period from July 1957 to April 1958. A comparison of the 2 outbreaks, based on the results of virus studies and the relevant statistical records, is the subject of the present paper.

The major epidemic developed at a season when respiratory diseases are relatively infrequent in average years but laboratory studies demonstrated that the majority of these illnesses were primarily or secondarily attributable to influenza. "The magnitude and rapid subsidence of the autumn epidemic suggested that a

majority of the population had gained immunity through infection." In the second wave of activity influenza "contributed only a small proportion of the respiratory illnesses which occurred" and observations from "general practice indicated that this second wave of influenza was virtually confined to those who escaped during the first wave". *M. E. Delafield*

TWEEDY, P. S., BEALE, A. J. & CAMPBELL, W. **The Diagnosis of Influenza: a Clinical and Serological Study.** *Med. Officer.* 1959, Nov. 6, v. 102, No. 19, 235–7, 1 fig.

During the early part of the 1957 influenza epidemic the outbreak was studied by clinical and serological methods in order to try to establish clear clinical syndromes. In the second part cases were diagnosed clinically before serological results were known: clinical and laboratory results were later compared. It is clear that laboratory diagnosis sharpened clinical judgment but that clinical diagnosis could in the later stages of the outbreak be made with reasonable accuracy. Thus of 59 patients showing 1 of the 3 syndromes considered most likely to be influenzal, 50 were confirmed as suffering from influenza by serological results but in no clinical category was correlation with serological results perfect. *A. B. Christie*

NICOD, J. L. & PROD'HOM, S. A propos de l'épidemie de grippe de 1957. Étude anatomo-pathologique. [**The Influenza Epidemic of 1957—an Anatomico-Pathological Study**] *Schweiz. Med. Woch.* 1959, July 11, v. 89, No. 28, 731–6. [Numerous refs.]

10 fatal cases of Asian influenza arising during the epidemic of 1957 were studied in Berne. They are divided into 3 groups according to the duration of the illness: (1) deaths within 3 days of onset—4 cases, (2) deaths between the 4th and 11th days—3 cases, and (3) deaths after the 18th day—3 cases.

Group (1) formed a clinical and pathological entity. The patients were all in good health when attacked by influenza, the course was rapid, and there was sudden unexpected collapse (convulsions in a child of 7); at autopsy the most conspicuous finding was haemorrhagic pulmonary oedema, and both the virus and *Staphylococcus aureus* were found in the 3 cases in which the examination was possible.

Group (2) was characterized by the autopsy finding of characteristic tracheo-bronchitis with replacement or necrosis of the cylindrical ciliated epithelium. *Staphylococcus aureus* was cultured from the lungs in all 3 cases, and there was serological evidence of infection with the virus of influenza.

In group (3) 1 patient aged 34, previously in good health, died of bronchopneumonia and pneumococcal meningitis, and 2 elderly patients with chronic chest disease died of bronchopneumonia in which both *Staphylococcus aureus* and the influenza virus were concerned.

The anatomical changes in these 3 groups thus reflect the duration of the illness, and the frequent occurrence of staphylococcal infection complicating the influenzal disease in fatal cases is worthy of note. [The latter has been frequently reported by other workers.]

*H. Stanley Banks*

WILSON, Miriam G., HEINS, H. L., IMAGAWA, D. T. & ADAMS, J. M. **Teratogenic Effects of Asian Influenza.** *J. Amer. Med. Ass.* 1959, Oct. 10, v. 171, No. 6, 638–41. [12 refs.]

An attempt was made to compare two groups of pregnant women whose last menstrual period was in October, November or December 1957—those with positive haemagglutination-inhibition titres against influenza virus and those with negative. Abnormalities in offspring were correlated with the haemagglutination-inhibition titre. No significant difference between the groups was found. *A. B. Christie*

MEDICAL RES. COUNCIL. BRITISH TUBERCULOSIS ASS. **Field Trial of Influenza Virus Vaccine in Patients with Chronic Bronchitis during the Winter 1957–8.** Report by the Joint Working Party of the Medical Research Council's Committee on Influenza and other Respiratory Virus Vaccines and of the Research Committee of the British Tuberculosis Association. *Brit. Med. J.* 1959, Nov. 7, 905–8.

The relative effects of 3 influenza virus vaccines were studied among 2,542 (1,943 males and 599 females) patients suffering from chronic bronchitis. A polyvalent influenza A vaccine with equal proportions of swine, PR8 and FM1 strains, an influenza B (1954) vaccine and a monovalent Asian influenza vaccine were compared. Each volunteer received a single subcutaneous dose of vaccine containing a total of 20,000 haemagglutinating units. A group of volunteers was vaccinated in September–October 1957 and another group in December of the same year.

Attack rates of bronchitis or other respiratory illnesses were not significantly different among the 3 vaccine groups. Protection against influenza was detected among men inoculated with the monovalent Asian vaccine in September–October but not among women vaccinated at the same time or among any of the subjects vaccinated in December. This apparent lack of protection may have been due to difficulties in reaching a correct diagnosis or to the relatively small number of women (110) vaccinated against Asian influenza in September–October.

No significant differences in mortality rates were detected among the 3 vaccine groups. *H. G. Pereira*

TYRRELL, D. A. J., BYNOE, M. L., PETERSEN, K. B., SUTTON, R. N. P. & PEREIRA, Marguerite S. **Inoculation of Human Volunteers with Parainfluenza Viruses Types 1 and 3 (HA 2 and HA 1).** *Brit. Med. J.* 1959, Nov. 7, 909–11. [11 refs.]

The effect of intranasal administration of parainfluenza viruses type 1 (HA 2) and type 3 (HA 1) was tested in volunteers kept in strict isolation. A strain of parainfluenza type 1, isolated in Denmark, and 2 strains of parainfluenza type 3, isolated in Britain were

employed. 9 of 18 volunteers given parainfluenza type 1 in doses ranging from 1·5 to 150 TCD50 showed evidence of infection and 6 of these developed symptoms consistent with a diagnosis of common cold. No evidence of infection was presented by 3 additional volunteers given a virus inoculum previously neutralized by specific immune serum. 8 of 20 volunteers given parainfluenza type 3 virus in doses ranging from 15 to 150,000 TCD50 showed evidence of infection with clinical symptoms of common cold (6 volunteers), influenza (1 volunteer) or with no symptoms (1 volunteer).

Virus was recovered from throat washings of all 9 volunteers infected with parainfluenza type 1 virus. Virus was also recovered from 6 of the 8 volunteers infected with parainfluenza type 3 virus.

Antibody responses were detected by virus neutralization, complement-fixation and haemagglutination-inhibition tests but a proportion of infected volunteers showed antibody rises which could be revealed by only 1 of these 3 tests. *H. G. Pereira*

See also p. 133, Löfgren & Callans, **Asian Influenza and Pulmonary Tuberculosis.**

Kawai, K. **Pathology and Pathologic Anatomy of Adenovirus Infection. Based on Three Autopsy Cases of Infantile Pneumonia.** *Japanese J. Exper. Med.* 1959, Aug., v. 29, No. 4, 359–68, 18 figs. on 3 pls. [23 refs.]

The English summary appended to the paper is as follows:—

"1. Pathology and pathologic anatomy of fatal infantile pneumonia due to adenovirus infection were described in three cases which were recently obtained in Japan.

"2. It is confirmed that the essential histopathological features of lower respiratory infection due to this virus were severe tracheitis, bronchitis and bronchiolitis with degeneration and necrosis of the epithelium characterized by specific intranuclear inclusion bodies.

"3. The characteristic developmental sequences of the intranuclear inclusion bodies in human tissue were described, and some differences between the cases were pointed out and discussed in relation to nuclear changes described in tissue cultured HeLa cells.

"4. Concerning the changes in the organs other than the respiratory tracts, descriptions were made especially of the lymph nodes, the tonsils, the intestinal mucosa, and based on the morphological changes; discussions were also made on suspected multiplication of the virus in some of these organs."

Jackson, A. L. & Louw, J. X. **Poliomyelitis at Birth due to Transplacental Infection.** *South African Med. J.* 1959, Apr. 25, v. 33, No. 17, 357–8.

"A case of intra-uterine poliomyelitis due to transplacental infection with Type 1 poliomyelitis virus is described.

"Part of the available literature on the transplacental transmission of poliomyelitis is summarized."

[See this *Bulletin*, 1956, v. 31, 702.]

Bloch, A. & Massry, S. [**Poliomyelitis and Measles in the Even-Shmuel Area**] *Harefuah.* Jerusalem. 1959, Oct. 1, v. 57, No. 7 [in Hebrew 180–82, 2 figs. English summary 182–3].

The English summary appended to the paper is as follows:—

"An epidemic of poliomyelitis affecting the Even-Shmuel area, Lachish, is described. 15 children contracted poliomyelitis of whom 4 died. Of the total number of children under the age of 4 in the settlements Uza and Eytan, 7 out of 93, and 5 out of 65 respectively actually developed the disease. This constituted the highest concentration of cases in the Ashkelon Region. Adjoining and neighbouring settlements were not affected in a like manner. An attempt was made to explain this on epidemiological and clinical grounds. The children had been followed up from birth and through their illness.

"The following factors were regarded as of no importance in the explanation of the selectively high incidence:—Age, country of origin of parents, overcrowding, inoculations with Salk vaccine, immunisation against diphtheria, pertussis and tetanus, vaccination, acute illnesses apart from measles, and the general state of health of the affected children.

"The epidemic of poliomyelitis was preceded by a severe epidemic of measles. Uza and Eytan had the severest epidemics of both illness. 12 out of the 15 children with poliomyelitis had contracted measles some weeks previously. Measles was regarded as an important positive factor, explaining the high selective incidence of poliomyelitis in the Even-Shmuel area.

"Of the 5 children known to have had severe anaemia, 4 contracted polio.

"The advisability of prophylaxis with gamma-globulin in high doses at the onset of a severe poliomyelitis epidemic in the special conditions pertaining to the Israel rural settlement, is discussed."

Nicolau, S. S. Date si consideraţii asupra relaţiilor de paraimunitate între poliomielită si herpes. [**Data and Considerations on the Relations of Para-immunity between Poliomyelitis and Herpes**] *Studii si Cercetări Inframicrobiol., Micriobiol. si Parazitol.* 1958, v. 9, No. 3, 293–314. [75 refs.] French summary.

55 children aged 11 months to 11½ years suffering or convalescent from poliomyelitis were inoculated by dermal scarification with herpes virus in the form of human vesicle fluid or infected rabbit brain. A herpetic lesion developed in 8 of 10 children inoculated between the 10th and 28th days of illness, in 5 of 12 inoculated between the 28th and 68th days and in 1 of 25 inoculated 68 days to 7 years after the onset of illness. As the result of these observations the author suggests that there is some degree of para-immunity between herpes and poliomyelitis. *D. J. Bauer*

FERGUSON, J. K. W. **Vaccination against Poliomyelitis with Combined Antigens.** *Canadian J. Pub. Health.* 1959, Sept., v. 50, No. 9, 385–9. [11 refs.]

The Director of the Connaught Medical Research Laboratories in Toronto described at meetings he attended in Vienna and Greece early in 1959 the combined vaccines which his laboratories have recently introduced. The early history of poliovaccination in Canada is briefly reviewed. There is now every confidence among the public health authorities in the safety and efficacy of poliovaccine. The main brunt of paralytic poliomyelitis, for example, in Manitoba in 1958 was borne by the least vaccinated age groups, 0–4 years and 20–39 years. In Canada nearly all children are protected against diphtheria, whooping cough and tetanus starting at 3 months of age. Poliovaccine has been added to this DPT vaccine (which is normal poliovaccine with $15 \times 10^9$ *Haemophilus pertussis* organisms, 40 Lf of diphtheria toxoid and 8 Lf of tetanus) and is used in 3 doses 1 month apart. 6–12 months after the first course a booster dose is given. A reinforcing dose of the DPT poliovaccine is recommended 2 years later. After the age of 5, pertussis is omitted and the doses of diphtheria and tetanus toxoids are reduced to 10 Lf. A combined tetanus-polio prophylactic has been prepared for use for adult immunization. Industrial medical officers have always thought it wise to give active immunity to tetanus but have found a lack of enthusiasm for the vaccination. The addition of poliovaccine has been found to sugar the pill, and cause the combined vaccine to be well received.

The detailed antibody response of young children to the Connaught combined antigens is promised soon. In summary the results show that after the first booster dose over 90% have antibodies to types 2 and 3 poliovirus and 85% to type 1. All children respond to diphtheria and tetanus immunization. Ferguson notes that these results fall short of perfection, but states that improved poliovaccine should overcome the present difficulties. Nonetheless, he recommends this course of inoculations as a simple, practical programme for mass immunization of young infants. He also refers in passing to the valuable micro method of poliovirus antibody determination developed by his colleague FARRELL [FARRELL & REID, this *Bulletin*, 1959, v. 34, 690] which is applicable to mass surveys in children. In Canada provocation poliomyelitis has not been noted [PEACH & RHODES, this *Bulletin*, 1955, v. 30, 13]; this is thought to be due to the absence of adjuvants in Canadian DPT vaccine.

[The schedule of combined vaccine administration recommended by Ferguson and implemented almost uniformly throughout Canada has many merits. It provides a simple, limited series of inoculations which give protection against 4 serious diseases. Since the Connaught Laboratories provide most of the prophylactics and vaccination is well-nigh universal it is possible to predict from a child's age the vaccine course which has been given. The use of combined vaccines does not lessen the need for improved poliovaccine, but does overcome some of the administrative difficulties and expense.] *A. J. Beale*

SABIN, A. B. **Status of Field Trials with an Orally Administered, Live Attenuated Poliovirus Vaccine.** *J. Amer. Med. Ass.* 1959, Oct. 17, v. 171, No. 7, 863–8. [18 refs.]

Sabin's latest review of the status of attenuated poliovaccine was delivered before the Ninth International Congress of Pediatrics in Montreal on 22 July, 1959. He reviewed briefly the evidence that administration of attenuated polioviruses by mouth did not cause any illness, that the virus multiplies in the alimentary tract of susceptible persons and gives rise to an immune response. Interference with the establishment of alimentary infection occurs when the 3 strains of virus are administered together and sometimes when other viruses are particularly prevalent in the community. There is clear evidence that the attenuated viruses can spread widely to the contacts of the vaccinated persons. Several studies have shown that the attenuated strains after passage in the human alimentary canal may be of greater virulence for monkeys than the original vaccine strains. These changes in neurovirulence of excreted viruses are not considered to be serious but it is stated that their real significance can only be determined in large scale field trials in human populations containing many susceptible individuals.

Several large scale field trials are now under way with Sabin's strains of virus. There are 3 requirements for an adequate field trial. 1. A preliminary serological survey of the population; 2. a careful clinical and virological control of the vaccinated population; 3. an estimate of the serological response of the population. A trial conducted in Mexico appears to support the view that in sub-tropical and tropical areas of low hygienic standard the prevalence of other viruses in the alimentary tract is sufficiently great to prevent an adequate response to the administration of attenuated poliovaccine. Sabin suggests that this may be overcome by the administration of viruses to newborn infants. Big trials are also under way in Czechoslovakia and the U.S.S.R. In both these trials there was a large number of susceptible persons and only a small proportion of them were vaccinated with the attenuated strains. There was evidence that the virus spreads to the unvaccinated susceptible contacts.

As Sabin says, the results of the trials in Czechoslovakia and the USSR will be awaited with interest. The most recent information would appear to show that they have proved that the attenuated poliovaccine is safe both for the individuals vaccinated and also for the community. Sabin believes that in view of the failure of Salk vaccination to eliminate paralytic poliomyelitis in the United States and Canada (mainly due to the inadequate acceptance of poliovaccination) the authorities should make available for mass immunization attenuated strains of poliovirus which could be used if the trials being carried out in Czechoslovakia and the U.S.S.R. confirm their early promise. *A. J. Beale*

CHRISTENSEN, C. N. **Reactions to Poliomyelitis Vaccine.** *J. Amer. Med. Ass.* 1959, Oct. 17, v. 171, No. 7, 869–72. [13 refs.]

The incidence of complications of poliovaccination reported to Messrs. Eli Lilly & Co. who have sold

more than 184 million doses is reported. There was a total of 284 complaints, 138 of which were of pain on injection. 56 of the remaining 146 reactions were various allergic manifestations, and 37 were of various neurological manifestations. Excluding the complaints of pain, the incidence of complaints reported to the manufacturer was of the order of 1 in a million. There were 6 cases of poliomyelitis following poliovaccination but in none of these was there evidence that the poliovaccine was responsible. The extremely low incidence of reactions to poliovaccine is stressed. Moreover, of the reactions that did occur, it is by no means clear that they were due to the poliovaccine. This is true even of the allergic manifestations because in relatively few of these were investigations carried out to establish whether or not the sensitivity was due to some component of the poliovaccine. *A. J. Beale*

VANĚK, J., LUKES, J., POTUZNÍK, V., POLEDNÍKOVÁ, I. & VILÍM, V. **Myocarditis and Encephalitis in Newborn Infants, caused by Coxsackie B Virus.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 283–91, 4 figs. on 2 pls. [10 refs.]

An epidemic of neonatal myocarditis involving 5 infants under 8 days is described. Coxsackie B 3 was isolated from the 1 fatal case. The pathological findings in this case and 3 other sporadic cases are described, showing typical necrotic myocarditis and in 2 of the 4 infants signs of encephalitis. The authors suggest that the disease can be recognized clinically by pallor, rapid pulse and enlarged heart and liver. They also suggest that routine histological examination of the myocardium might reveal more sporadic fatal cases. *A. J. Beale*

LYLE, W. H. **An Outbreak of Disease believed to have been caused by ECHO 9 Virus.** *Ann. Intern. Med.* 1959, Aug., v. 51, No. 2, 248–69, 14 figs. [13 refs.]

A full account of an epidemic affecting 162 persons in Newton-le-Willows, Lancashire, in June 1956 is presented. Special emphasis is given to the clinical picture. 2 distinct types of illness were seen in children and in adults, but on epidemiological grounds were taken to be manifestations of the same infection. The disease affected several members of a family. In children the disease was usually milder, with headache, nausea, sometimes with vomiting, and fever. A blotchy, macular, bluish-red rash was seen in 50% of the patients. A quarter of the patients had neck stiffness, but muscle weakness was not found. A few patients had sore throat with vesicles, petechiae or ulcers on the palate. The disease was severe in adults with headache, fever and severe muscular pain in the limbs. Patients with severe headache, limb pains, photophobia and vomiting were relieved by lumbar puncture. Neck stiffness was rare and rash was uncommon. Definite muscle weakness was seen in some patients. Although the disease was of short duration (under 2 weeks) low grade recurrence and a prolonged period of convalescence with fatigue and weakness and pain in the limbs coming on during the day occurred.

The virus studies were unfortunately not extensive but clearly suggest that the outbreak was due to ECHO 9 virus.

9 detailed case-histories are given. *A. J. Beale*

WARIN, J. F., IRONSIDE, A. G. & WIGFIELD, W. J. **Non-Bacterial Meningitis in Oxford, 1957.** *Med. Officer.* 1959, Aug. 28, v. 102, No. 9, 85–6, 2 figs.

An outbreak of non-bacterial meningitis occurred in Oxford in the summer of 1957. The symptomatology was similar to that occurring in meningitis due to ECHO type 9 virus, but no virus was recovered from any of 19 faecal cultures. Paired sera likewise gave no indication of possible viral aetiology. *A. B. Christie*

BÁRDOS, V. & ROSICKÝ, B. **Natural Foci of some Virus Infections of Man in Slovakia.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 237–48. [92 refs.]

This is the first of a series of papers on the occasion of the 75th birthday of E. N. PAVLOVSKY and illustrates the application of his theory of natural foci of infections to problems of virus diseases in Czechoslovakia. Natural foci of Russian spring-summer encephalitis in Central Europe occur in 5 type-situations: (1) Theriodic foci: in tick-infested forest, often artificially planted and containing game preserves. Sporadic infections of foresters, holiday-makers etc. occur. (2) Boskematic foci: in tick-infested pastures which may be surrounded by woods or scrub. Infection of man is mainly milk-borne from infected goats and sheep and may occur in epidemics, especially family epidemics. (3) Theriodic-boskematic foci: in situations where (1) and (2) are intermingled. (4) Mountain foci in which tick infestation is low and in which human infections are rare. (5) Catarchaic foci in virgin territory.

Eastern equine encephalomyelitis virus has been isolated from ticks and forest rodents. Antibodies have been found only in cattle and these findings need further investigation.

Lymphocytic choriomeningitis virus has been isolated from house mice and from *Apodemus flavicollis*. As human infections occur in winter it is believed that infection is introduced into houses by field mice wintering in them.

The Tahyna virus was isolated from mosquitoes [see BARDOS and DANIELOVA, p. 207 below] and antibodies have been found in man and horses. It is associated with marshes and perhaps with the birds which frequent them. Maximum incidence coincides with the time when young birds leave the nest.

Antibody studies in man and domestic animals suggest that a virus related to western equine encephalomyelitis exists in Czechoslovakia [but this must be accepted with caution]. Antibodies to encephalomyocarditis virus have been found in man, rats, horses, cattle and pigs. It appears to affect mainly rural inhabitants working in stables.

Haemorrhagic nephroso-nephritis is believed to occur and investigations—so far negative—are in progress.

[This is a useful review of virology in Czechoslovakia, particularly the list of 92 references.]

*C. E. Gordon Smith*

ROSICKÝ, B. & HEJNÝ, S. **The Degree of Cultivation of a Region and the Epidemiology of Natural Foci of Infection.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 249–57. [45 refs.]

This is the second paper in honour of PAVLOVSKY's birthday. 5 stages of cultivation are distinguished in Czechoslovakia. (1) Areas without human interference which scarcely now occur in Europe. (2) Slightly cultivated areas where natural forest etc. is interspersed with pastures. Leptospirosis and Russian spring-summer encephalitis may be important in such areas. (3) Moderately cultivated areas where there are mosaics of different types of forest (natural and artificial) and cultivated land. Draining and irrigation are important. Tularaemia may be greatly diminished by draining of marshes. Preservation of large numbers of game animals on the other hand may maintain tick-borne encephalitis. (4) Highly cultivated regions where the land is largely cultivated or partly cultivated, but islands of the original vegetation remain, where *e.g.* leptospirosis and tick-borne encephalitis may persist. (5) Completely cultivated areas. *C. E. Gordon Smith*

BÁRDOS, V., ADAMCOVÁ, J., DEDEI, S., GJINI, N., ROSICKÝ, B. & ŠIMKOVÁ, A. **Neutralizing Antibodies against some Neurotropic Viruses determined in Human Sera in Albania.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 277–82. [26 refs.]

112 human sera were collected from 3 areas in Albania. They were tested for neutralizing antibody to Russian spring-summer virus (strain "O" from Czechoslovakia), West Nile virus (Egypt 101), Tahyna virus and encephalomyocarditis virus. Inactivated sera were tested in pools of 3 against 10–50 LD50 and the individual sera in positive pools were retested. 4 sera were found with Russian spring-summer, 2 with West Nile, 2 with Tahyna and 13 with encephalomyocarditis antibody. *C. E. Gordon Smith*

LACHMAJER, Jadwiga; SKIERSKA, Barbara; WEGNER, Zofia. **Characteristics of a Natural Focus of Encephalitis Viruses in the Neighbourhood of Kartuzy (Gdansk Province) 1957. I. Fauna Ixodidae and Culicidae from the Kartuzy Region** [LACHMAJER & SKIERSKA]. *Bull. Inst. Marine Med. Gdańsk.* 1959, v. 10, Nos. 3/4, 165–73, 2 graphs. [12 refs.] **II. Small Mammals and their Ecto-Parasites in the Neighbourhood of Kartuzy** [LACHMAJER & WEGNER]. *Ibid.*, 175–84. [15 refs.]

I. The study was made in a hilly area near the Baltic Sea with woods, bogs and lakes. Ticks were collected from cattle and in the woods, and mosquitoes in the woods and in farm buildings. Ticks were caught by dragging "flags" on vegetation—all were *Ixodes ricinus*. The maximum activity of the ticks was in June with a smaller peak in early September. 81% of the ticks caught in the woods were nymphs, 98% of those caught on cattle were adult females. 80% of the mosquitoes caught in the woods in May to July were *Aëdes communis*; in August and September 40% were *Aëdes communis* and 34% *Aëdes cinereus*. Mosquitoes were taken from the beginning of May to the middle of September, but were numerous only in June. *Aëdes communis* attacked men from 4 a.m. till 11 p.m. In farm buildings *Anopheles maculipennis* and *A. bifurcatus* predominated.

3,983 ticks were inoculated into mice and two strains of virus were isolated from ticks off cows. The viruses have not yet been identified. No viruses were isolated from the mosquitoes.

II. In the woods the commonest animals trapped were *Clethrionomys glareolus* (56%), *Microtus arvalis* (11%), *Sorex araneus* (11%) and *Apodemus flavicollis* (8%); in fields and gardens they were *Mus musculus* (43%), *Apodemus agrarius* (28%), *A. flavicollis* (15%) and *Rattus norvegicus* (12%); indoors 97·5% were *Mus musculus* and the rest *A. agrarius*.

Of 2,047 ectoparasites 29% were lice (Anoplura), 9% fleas (Aphaniptera) and 61% Acarina (58% mites and 3% ticks). 31% of the animals had lice, *C. glareolus* being most heavily infested, and *Mus musculus* least. *Hoplopleura acanthopus* and *Polyp'ax serrata* were the commonest species of lice. A strain of virus was isolated from *Hoplopleura affinis* off *A. agrarius*. *C. glareolus* was most heavily infested with fleas, the commonest species being *Ctenophthalmus agyrtes*. 60% of the animals were infested with mites: *C. glareolus* and *A. flavicollis* were most heavily infested. *Ixodes ricinus* and 2 other *Ixodes* spp. were taken. *I. ricinus* was found on 5 species of birds and 7 species of small mammals. [This paper contains a wealth of detail on the ectoparasites of the small mammals trapped.]

*C. E. Gordon Smith*

IGOLKIN, N. I., VERSHININA, T. A. & FEDOROV, Y. V. **[The Part of Gamasoidea Mites in the Epizootology of Tick-Borne Encephalitis]** *Med. Parasit. & Parasitic Dis.* Moscow. 1959, v. 28, No. 5, 568–71. [In Russian.]

The English summary appended to the paper is as follows:—

"No virus could be detected following virological investigations of 5412 Gamasoidea mites collected from the nests of small mammals within the nidi of tick-borne encephalitis.

"Experimental investigations involving feeding of the mites on the blood containing the virus of tick-borne encephalitis proved the terms of virus survival in the mite's body to be as follows: for Haemogamasus mandschuricus Vitzth.—up to 7 days; Eulaelaps stabularis (C. L. Koch) up to 18 days; Haemolaelaps sp—14 days, Haemolaelaps casalis (Berl.)—3 days and Haemolaelaps glasgowi Ewing—up to 12 days."

SULLIVAN, Thelma D., GRIMES, J. E., IRONS, J. V. & PEAVY, J. E. **Lower Rio Grande Valley Outbreak of St. Louis Encephalitis.** *Texas Reports on Biol. & Med.* 1959, v. 17, No. 3, 439–43.

This is an account of laboratory tests on patients in an outbreak of 120 cases in the summer of 1957.

Of 33 patients with clinical encephalitis, 4-fold or greater rises in St. Louis complement-fixing antibody were demonstrated in 14. No response was found in any when tested against western and eastern equine encephalomyelitis and lymphocytic choriomeningitis antigens. In sera from 426 people who were presumably exposed to infection but were not ill, 30% had St. Louis complement-fixing antibody.

1,900 mosquitoes, 85% of them *Culex quinquefasciatus* [*fatigans*], were tested for virus. St. Louis virus was isolated from 8 of 40 pools of *C. quinquefasciatus*.

*C. E. Gordon Smith*

GALINDO, P., DE RODANICHE, Enid & JOHNSON, C. M. **St. Louis Encephalitis in Panama. I. Isolation of the Virus from Forest Mosquitoes and Human Blood.** *Amer. J. Trop. Med. & Hyg.* 1959, Sept., v. 8, No. 5, 557–60, 1 fig. [12 refs.]

Mosquitoes coming to bite man were trapped on platforms in the forest canopy in 3 areas: (1) Buena Vista on the Atlantic slopes of the Continental Divide; (2) Paya near the Colombian border in the Province of Darien; (3) Tacarcuna on the slopes of Mount Tacarcuna in Darien. Mosquitoes were kept alive for 24–72 hours at room temperature then sent on ice to Panama City for processing. Adult mice were used for mosquitoes from Buena Vista and suckling mice for the others. Isolations of St. Louis virus from mosquitoes were as follows: Buena Vista, July 1957 from a pool of 95 *Sabethes chloropterus*; Paya, June 1958 from 133 *S. chloropterus*; Paya, July 1958 from a pool of 139 *Sabethes* of at least 5 species other than *chloropterus*; Paya, August 1958, from 153 *S. chloropterus*; Tacarcuna, September 1958, from 114 *S. chloropterus*. Isolations were also made from the blood of a mosquito catcher at Paya in February 1958 and from another in September 1958. The symptoms were fever, headache and retro-orbital pain. In one of these patients only, a significant rise in antibody level in convalescence was demonstrated.

The identity of one virus strain was proved by cross-complement fixation, cross-neutralization and cross-challenge experiments. The other strains were then shown to be identical with it. A number of other strains of virus related to St. Louis virus were isolated, but not described in this paper. *C. E. Gordon Smith*

PAPP, Karola. Explication du pathomécanisme de la rougeole. [**An Explanation of the Mechanism of Pathogenesis of Rubella**] *Rev. d'Immunologie.* 1959, Jan.–Mar., v. 23, Nos. 1/2, 97–113. [40 refs.]

On the basis of previous work and clinical observations [this *Bulletin*, 1955, v. 30, 941; 1959, v. 34, 969] the author has developed a hypothesis of the pathogenesis of rubella. It is postulated that the virus enters through the conjunctiva and multiplies inside the leucocytes in the circulating blood without producing any symptoms. The virus also liberates a soluble antigen; antibody to this is formed, and in combining with antigen liberates a toxin which then produces the manifestations of the disease. *D. J. Bauer*

LEE, Ti-Kai & HSU, Cheng-Jen. [**Rubella Encephalitis**] *J. Formosan Med. Ass.* 1959, May 28, v. 58, No. 5, 277–85. [11 refs.]. [In Chinese.] English summary.

A report of 3 cases.

PERRIER, C. V. & ROUSSO, C. Un cas de mononucléose infectieuse avec anémie hémolytique et test de Coombs positif. [**A Case of Infectious Mononucleosis with Haemolytic Anaemia and Positive Coombs Test**] *Schweiz. med. Woch.* 1959, July 18, v. 89, No. 29, 766–9, 2 figs. [18 refs.]

The case of a girl of 19 is described with infectious mononucleosis, characterized clinically by adenopathy, angina, and enlarged spleen, and after laboratory tests, by anaemia, lymphocytosis, monocytosis, and positive Paul-Bunnel-Davidsohn reactions. 3 weeks after onset she was found to have haemolytic anaemia with positive Coombs test, direct and indirect, and 2 weeks later the cold agglutinin test was positive. The anaemia reacted favourably to steroid treatment. The mechanism of production of the haemolytic anaemia is discussed, and the view favoured that auto-immunization was involved, antigens on the surface of the red corpuscles being activated or formed by means of viral enzymes.

The condition is rare; 17 cases, all in children and young adults, are cited from the literature, in all but 2 of which the spleen was enlarged.

*H. Stanley Banks*

SHIPP, J. C. & BADEN, H. **Leukemoid Reaction in Infectious Mononucleosis. An Infrequent Manifestation simulating Leukemia.** *Arch. Intern. Med.* 1959, Oct., v. 104, No. 4, 619–21, 1 fig.

"An instance of infectious mononucleosis in an 18-year-old student associated with a transient leukemoid reaction (leukocyte count over 50,000 per cubic millimeter) is reported. The leukocytosis consisted largely of lymphocytes; many of the atypical lymphocytes simulated "blast" forms. This feature in a less characteristic clinical setting may suggest leukemia, especially when associated with bleeding manifestations, anemia, adenopathy, and splenomegaly. The causes of lymphocytic leukocytosis are reviewed."

KURZWEIL, H. Vorsichtsmassnahmen bei der Herstellung keimfreier Blutkonserven während einer Epidemie. [**Precautions in the Collection of Sterile Blood for Transfusion during an Epidemic**] *Deut. med. Woch.* 1959, Oct. 23, v. 84, No. 43, 1942–8, 1956. [18 refs.]

Apart from the relatively numerous published papers on the possible dangers of the spread of certain infections, particularly hepatitis, syphilis and malaria by blood transfusion, little is known of the difficult situation which may arise during a large epidemic of other infectious diseases in regard to blood donors who may be in the incubation period of the infection.

There is a description of the general precautions which should be taken in building up a blood bank free of infection. An account is given of the experience of the author in this field during the very large epidemic of erythema infectiosum in Northern Germany in 1958.

The whole subject of the precautionary measures which should be taken in the blood transfusion service at all times and also when particular infections are epidemic in an area is tnen given very detailed description, discussion and the author's recommendations.

*M. E. Delafield*

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## OTHER COMMUNICABLE DISEASES

SULHEIM, O., DELGAARD, J. B. & ANDERSEN, S. R. **Behcet's Syndrome. Report of a Case with Complete Autopsy Performed.** *Acta Path. et Microb. Scandinavica.* 1959, v. 45, No. 2, 145–58, 12 figs. [32 refs.]

Behçet, a Turkish dermatologist, in 1937 first described a syndrome comprising oro-genital ulceration with eye changes, which is now known by his name. The authors discuss present knowledge of this condition and report a further case.

The syndrome is thought to be more common in the Middle East than in Europe; it attacks men more frequently than women and has its highest incidence between 15 and 40 years of age. Behçet observed inclusion bodies in smears of hypopyon fluid and in scrapings from oral ulcers and postulated a viral aetiology: this suggestion has not been superseded.

The oral lesions, which are painful, resemble aphthous ulcers; they occur on the tongue, palate and the buccal surface of the cheeks. The genital lesions in the male take the form of painful shallow ulcers on the scrotum and more rarely on the prepuce and glans penis. In the female deep ulceration of the vulva is common, though occasionally the vagina and cervix may be affected.

Eye lesions may dominate the clinical picture. They range from recurrent unilateral or bilateral iritis or iridocyclitis with hypopyon, while later retinitis, obliterative vascular changes, optic atrophy and secondary glaucoma may develop. Blindness not infrequently ensues. Other systems which may be involved are the skin, lungs, joints, central nervous system and blood vessels. [Many authorities stress the important role of thrombosis in the pathogenesis of the symptomatology of this strange disease.] The skin lesions included erythema multiforme, erythema nodosum and pyodermia; in the lungs pneumonia of almost any type may be found and in the nervous system a wide variety of syndromes—encephalitic, bulbar and meningomyelitic have been described.

Death may be due to the pulmonary or cerebral complications of the disease, or to the asthenia. Treatment is ineffective since vitamins, antihistamines, chemotherapy and antibiotics are of no avail.

The most characteristic feature of the condition [which should provisionally be accepted as a disease entity] is its tendency to relapse and to involve sequentially several different systems, though the intermissions are irregular and may last for several years.

The patient described in this paper was a widow of 59 years. Her illness began in 1956 with transient pulmonary inflammation, accompanied by much systemic disturbance. In early 1957 multiple skin ulcerations and a palatal ulcer developed; 2 months later cerebral involvement was evident. After a further 2 months' interval, bilateral irido-cyclitis and a vulval ulcer appeared. She then showed a right-sided hemiparesis with dysarthria, her blood showed a mild hypochromic anaemia (Hb. 10·6 gm./100 ml., MCHC 24%) and in her serum the gamma globulin was much increased. On X-ray both lungs showed disseminated opacities resembling a fungal or viral pneumonia. The dermal, oro-genital, ocular and pulmonary lesions steadily became more intense and led to her death from general asthenia in October, 1957, 18 months after the first recognizable symptoms and 8 months from the beginning of the final phase of her disease.

*J. H. Walters*

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# Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

*Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the* TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

## GENERAL

TUNEVALL, G. [Editor]. **Recent Progress in Microbiology.** Symposia held at the VII International Congress for Microbiology, Stockholm, 1958. Under the auspices of the International Association of Microbiological Societies IAMS and the Swedish Microbiological Society. With an addendum (in English and French) on the Structure and Function of IAMS compiled by C.-G. HEDÉN, Sec. Gen. 453 pp., numerous figs. 1959. Oxford: Blackwell Scientific Publications Ltd., 24–25, Broad Street. [70s.]

This well-produced volume contains presidential addresses by Sven GARD and Stuart MUDD, 6 symposia, and an addendum by C.-G. HEDÉN, Secretary General of the International Association of Microbiological Societies, in which he describes the structure and function of the Association. The subjects of the symposia are: I. Recombination mechanisms in bacteria; II. Role of protein in nucleic acid synthesis and role of nucleic acid in protein synthesis; III. Tissue specific antibodies; IV. Latent and masked virus infections; V. Germ-free animals; and VI. Continuous culture methods and their application.

*Symposium I: Recombination in bacteria*

F. JACOB and E. L. WOLLMAN (pp. 15–30) discussed the relationship between prophage and the bacterial chromosome in lysogenic bacteria. A clear exposition is given of a complex train of reasoning, the conclusion being that prophage attaches itself to the chromosome of *Escherichia coli* K12 at a specific point in the chromosome, and that the attachment is not by complete insertion into the line of genes: prophage is not substituted for a gene allele of the bacterium although it replicates with the rest of the chromosome.

B. A. D. STOCKER's account (pp. 31–39) of phage-mediated transduction drew attention to differences in behaviour between *Salmonella* phages and *E. coli* phage λ. In the latter system, phage progeny from one cell may contain numerous transducing particles, which must therefore themselves have replicated in the bacterium before lysis; in the *Salmonella*-P22 system, on the other hand, the transducing particle is a simple fragment of bacterial chromosome. Transducing phages resemble normal phages in size, sensitivity to ultraviolet light, insensitivity to deoxyribonuclease and antigenic specificity, but they do not carry a full complement of phage genes.

The bacterial genetic material transduced may not be fully incorporated into the bacterial chromosome and may not replicate, producing a phenotypic change in only one or a few daughter cells. This phenomenon is called "abortive transduction".

L. L. CAVALLI-SFORZA's presentation of current views on recombination (pp. 40–50) dealt with the difficult interrelationships of $F+$, $F-$ and *Hfr* forms and the problematical nature of the *F* factor. The paper is closely reasoned, and difficult to abstract usefully.

Harriett EPHRUSSI-TAYLOR's account (pp. 51–68) of the present position with regard to the mechanism of deoxyribonucleic acid-induced transformation is likewise too complex for useful abstract and should be studied *in extenso*. Its theme is what happens to the deoxyribonucleic acid after its entry into the competent cell, and its relation to that cell's genetic apparatus.

R. AUSTRIAN (pp. 69–71) described a doubly capsulated type I–III pneumococcus obtained by transformation, and discussed some of the genetically controlled biochemical activities related to capsular synthesis.

Others contributing to this symposium were G. BERTANI, W. BRAUN, P. FREDERICQ, W. SZYBALSKI and P. SCHAEFFER.

*Symposium II: Role of protein in nucleic acid synthesis and of nucleic acid in protein synthesis*

S. SPIEGELMAN (pp. 81–103) described experiments on fragments of *E. coli* protoplasts. Most active protein and nucleoprotein synthesis occurs in fragments representing protop'ast membranes, which possess more than 100 times the activity of the other fragments studied. Optimal conditions for synthesis of polyribonucleotide are defined.

E. F. GALE (pp. 104–114) discussed the nature of the early stages involved in the incorporation of amino-acids by bacteria and the role of "incorporation factors" in amino-acid incorporation and nucleic acid synthesis, as revealed by his experiments with disrupted staphylococcal cells. If nucleic acid is removed from the smashed cells, the power of amino-acid incorporation is lost, but may be restored either by restoring the nucleic acid or by an unidentified "incorporation factor" produced by treating the ribonucleic acid fraction with ribonuclease and subsequent partial purification. The system is studied in relation to pyrophosphate exchange.

In the subsequent discussion, E. HAMMARSTEN, D. B. COWIE, F. E. HAHN and M. BELJANSKI, took part.

S. OCHOA (pp. 122–138) described his great work on the biosynthesis of ribonucleic acid. It is unnecessary to abstract this paper in detail; it is a most valuable reference source, dealing with the mechanism of polynucleotide synthesis.

S. ZAMENHOF (pp. 139–146) discussed the correlation between changes in structure and function of DNA. The effect of various inactivating agents on the transforming DNA of *Haemophilus influenzae* is described. Various mutagens inactivate DNA or, if used "sublethally", produce instability to heat. True mutational change has not, however, been produced *in vitro*. In *in vivo* experiments, further evidence relating mutational change to change in DNA structure is presented.

F. GROS, E. VOLKIN, and the moderator, A. TISELIUS, joined the discussion.

*Symposium III: Tissue specific antibodies*

R. R. A. COOMBS (pp. 156–162) reviewed the techniques applicable to the detection and study of antibodies generally.

Ö. OUCHTERLONY (pp. 163–169) enlarged on his own technique of double diffusion of antigen and antibody in agar plates, derived from OUDIN's simple tube diffusion method, and mentioned the immune electrophoresis method of GRABAR and WILLIAMS.

P. GRABAR (pp. 170–180) discussed auto-antigenicity. He gave a historical account of the subject, then listed phenomena which have been classed as manifestations of auto-antibodies, and finally discussed some of the hypotheses which relate these phenomena to the main body of immunological ideas.

L. BRENT and P. B. MEDAWAR (pp. 181–190), on tolerance and auto-immune phenomena, provided a useful exposé of immune tolerance as a general phenomenon. They proposed 3 kinds of reason why antigens of native origin do not normally incite an auto-immune response: because they are constituents of the antibody-forming cells themselves; because they never reach the antibody-forming cells; or because the body is immunologically tolerant of them. Of these three, they regarded the third as the important one. Native antigens likely to provoke auto-antibody formation may be those against which it has not been possible for tolerance to be acquired.

E. WITEBSKY, P. MIESCHER, K. O. VORLAENDER and F. MILGROM contributed to the discussion.

*Symposium IV: Latent and masked virus infections*

A. LWOFF, on "latency at the cellular level and the three body problem" (pp. 211–217), drew examples from animal, plant, insect and bacterial viruses. His 3 "bodies" are organism, cell and virus; and he emphasized, partly from his own work on temperature, that the behaviour of the virus is largely conditioned by the behaviour of the cell it lies in and of the organism of which that cell is a part. He also drew attention to the danger of generalizing from one "three body" system to others.

C. W. BENNETT, on "masked plant viruses" (pp. 218–223), attempted first to define terms. In present context, "masked", "latent", "inapparent", "subclinical" [!] and "occult" all seem to mean much the same thing. Bennett reviewed many of the known facts about masked plant viruses, and considered that there is little evidence that masking is due to suppressants or inhibitors; but that more probably the appearance of symptoms may depend on the concentration of virus that can develop in the cell. The factors determining this concentration are obscure.

K. MARAMOROSCH (pp. 224–229) listed and discussed some of the very interesting phenomena of latent virus infection in insects.

R. E. SHOPE'S account of latent virus infections in animals (pp. 230–237) recounted the extraordinary biological organizations which he has revealed in his well known work on swine influenza and hog cholera. His discussion brought out the important distinction between viruses which may be latent in infective form, even if in small quantity, capable of detection in infectivity tests, and those which, like swine influenza and hog cholera, may be truly "masked" in that, in their latent form, their infectivity cannot be revealed by simple inoculation into susceptible hosts, but only after "provocation" [a process bearing at least superficial resemblance to "induction" of phage in lysogenic bacteria].

R. DULBECCO, H. R. MORGAN, K. M. SMITH, E. TRAUB and T. H. WELLER contributed to the discussion. Morgan described latency of psittacosis virus in tissue cultures. Weller presented the peculiar and, perhaps, "key" case of varicella virus. The papers in this symposium stimulated a very vigorous discussion, too long to abstract in detail. which was summed up by F. M. BURNET who posed a number of provocative questions.

*Symposium V: Germ-free animals*

The main contributors to this symposium were J. A. REYNIERS, P. GYÖRGY, M. MIYAKAWA, W. H. WRIGHT, B. P. PHILLIPS and W. L. NEWTON, and B. GUSTAFSSON. The earlier papers were largely concerned with the technique, chiefly developed by Reyniers at the Lobund Institute, Indiana. Topics investigated with this technique include the dietary effect of antibiotics on young animals (chiefly due to antibacterial action, and therefore less marked in germ-free animals); healing and the inflammatory process, infection with *Entamoeba histolytica*, nematode parasites and *Trichomonas*.

Gustafsson's contribution, dealing with germ-free rats, described caecum enlargement and its mechanism, serum protein distribution, vitamin K deficiency, metabolism of cholesterol, bile acids and bile pigments, the output of enzymes in faeces and the distribution of histamine in tissues. Normal rats produce about 3 times as much gamma globulin as germ-free rats, suggesting that the microbial flora has something to do with stimulating the antibody-producing mechanism. No difference in histamine distribution was found between germ-free and normal rats.

H. A. GORDON and B. S. WOSTMANN (pp. 336–339) showed that the lymphoid tissues of germ-free animals are very poorly developed. T. D. LUCKEY (pp. 340–349) discussed antibiotic growth stimulation, and concluded that part of the effect may be due to direct action of the antibiotic on the animal, independent of microbial action.

T. G. WARD, and others, contributed to the discussion.

*Symposium VI: Continuous culture methods and their application*

V. BRYSON (pp. 371–380) described a turbidistat and discussed its use in the selection of mutants in continuous culture. D. HERBERT (pp. 381–396) described a chemostat, and discussed the differences in principle and performance between chemostats and turbidistats. He described several aspects of growth in continuous culture, treating them where possible mathematically. Changes in growth rate, substrate concentration, cell size and the relative concentrations of different cell constituents present a fascinating array of changing dynamic interrelationships. M. J. JOHNSON (pp. 397–402) discussed rates of oxygen utilization by micro-organisms. A. NOVICK (pp. 403–415) discussed the working of the chemostat, and its advantages, especially in the study of the accumulation of mutants and for experiments in which a rapidly consumed metabolite is kept at a low concentration. W. E. BROWN, P. GERHARDT, F. GRAZIOSI, T. HOLME, E. O. POWELL and others took part in the discussion. P. D. COOPER described experiments on continuous culture of mammalian tissue cells.

[DESCARTES wrote that "*la lecture de tous les bons livres est comme une conversation avec les plus honnêtes gens des siècles passés qui en ont été les auteurs, et même une conversation etudiée, en laquelle ils ne nous découvrent que les meilleurs de leurs pensées*". The contributors to these symposia included many of the most distinguished microbiologists of the present century, and their communications are of great interest. But ought they to be asked to allow their communications to be printed in this form? The word "symposium" suggests the relaxed informal atmosphere of friends dining together. Those participating should feel free to reveal the thought of the moment without scrutinizing it to see if it is bookworthy. One advantage of a symposium is that it gives opportunity for "stop press" communication and discussion: this quality has faded by the time that an expensive volume of verbatim minutes has been edited, printed and published. The present volume suffers from the many pages of small print transcription from the tape recorder; much of this is trivial, unconsidered comment, the life of a good discussion, but the death of a good book. Contributions to symposia are allotted, necessarily, so many minutes of speaking time. Some in this volume are so compressed in their presentation that one can almost hear the closely written typescript turning over as the reader rushes to cram his spoken words into the prescribed time. Nearly all the important material has been or will be properly published in a form intended to be read, not spoken. Important though this material is, it can hardly be described as a book; and seventy shillings is a big price for the minutes of six unrelated meetings held a year ago. In short, the present reviewer feels more convinced than ever that verbatim records of symposia are better not published.] *E. T. C. Spooner*

THOMAS, J. André [Published under the Direction of]. Prob'émes d'organisation et de fonctions chez les bactéries et les virus. **[Problems of Structure and Function in Bacteria and Viruses]** pp. xii+386, 154 figs. 1958. Paris-VI$^{e}$: Masson et Cie., 120, Boulevard Saint-Germain. [5,000 fr.]

This is the fourth of a series of treatises on cell biology published under the direction of J. André Thomas.

The first two chapters by A. R. PRÉVOT deal with details of bacterial structure and with bacterial classification. The evidence for a bacterial nucleus and for sexual reproduction are specially considered and the position is adopted that we are justified in speaking of *appareil nucléaire* rather than of nucleus and that evidence for sexual reproduction has only as yet been satisfactorily established for some strains of *Bacterium coli.*

In the matter of classification, it is maintained that for species the enzyme and antigen patterns are the essentials, but that variations in equipment with enzymes is sufficient for differentiation of varieties and that for types the antigen composition, and immunochemical structure of toxin, are taken into account. An extended scheme of classification is set out in the second chapter in which special emphasis is put on anaerobic forms. This differs at many points from that adopted by BERGEY.

In the third chapter P. GIROUD and N. DUMAS discuss the forms which they gather under the general title "Infra-microbes". The two main groups considered are the Rickettsiales and Peripneumoniales. Under the former the 3 principal groups are the Rickettsiaceae, the Bartonellaceae and the Chlamydozoaceae. Under Chlamydozoaceae the agents of psittacosis, of trachoma and of lymphogranuloma are discussed, *i.e.* forms nearly related to the larger viruses.

Only the *Asterococcus mycoides,* agent of bovine pleuropneumonia, is discussed in the group Peripneumoniales.

In two further chapters, P. HAUDUROY surveys the difficult question of the appearance of filtering forms in the course of bacterial cycles of development and especially the bacteria of peripneumonia, the peripneumonia-like [pleuropneumonia-like] forms (PPLO) and the "L" phase in bacteria which appears so readily under the influence of penicillin.

In a general summary of this difficult field, he concludes that no filtering form derived in any of the cycles of changes described has ever been shown to possess the essential attributes of a virus, *i.e.* obligatory symbiosis with the living animal or plant cell.

There follow chapters by R. VENDRELY on the role of nucleic acid and nucleoproteins in the growth and reproduction of bacteria, and by J. BARRAUD on the methods of crystallography and their application to the structure of the virus. The latter goes into the evolution of this highly specialized method of investigation with many good illustrations which should be helpful to those with a limited knowledge of physics and of protein chemistry.

In the 8th chapter C. HANNOUN discusses the composition and function of viral antigens. The ideas first developed by HOYLE and his colleagues in relation to influenza virus, and subsequently confirmed and extended by LIEF and HENLE for that virus and supported by the work of SCHÄFER and others on fowl plague, are fully described. The conception is that of a virus appearing in different phases, the smallest and first to appear being antigenic and, in the case of the two viruses described, autoreproductive and becoming associated as a larger

particle with protein elements endowed with enzymic activities and responsible for the phenomenon of haemagglutination and, finally, by the further acquisition of lipid elements to constitute the complete virus particle which is infective.

In the last chapter, P. LÉPINE deals with the relationships of virus and cell, the inclusion bodies, and the important experimental advances presented by the technique of tissue culture artificially infected with virus.

Lépine feels that the question so long debated—whether the viruses are living or inanimate—is not one on which to spend much time since the virus can exist outside the cell as a substance no more complex than some known organic compounds, but can influence the cell in which it lodges to a change of composition and structure through an effect on the essential reproductive mechanism. It is suggested that the infection of cultures of living tissue by viruses is the nearest approach which man has yet made to experimental work on the mystery of life.

*J. W. McLeod*

HRADECNÁ, Z. Contribution à l'étude de la structure macromoléculaire du protoplasme bactérien. [**The Macromolecular Structure of Bacterial Protoplasm**] *C.R. Soc. Biol.* 1959, v. 53, No. 5, 890–93, 1 fig.

The following is a translation of the author's summary:—

It may be concluded from these experiments that destruction of bacterial protoplasm [*Escherichia coli*] by ultra-sonic waves is accompanied by the appearance of globules 200–350 Angstrom units in size. The filtrate containing these globules is able to produce transferable lysis of the bacterial cell.

These results, in addition to results obtained by other workers, suggest that these globules are not artificial structures, but are elements which form the bacterial protoplasm, liberated after the disruption of the cell by ultra-sonic waves. They have biological activity and are therefore not the products of degeneration. These properties may lead to elucidation of their activity and, through biophysical and biochemical study, of their role in the macromolecular structure of protoplasm.

*Charles Wilcocks*

SHEPARD, C. C. **Nonacid-Fast Bacteria and HeLa Cells: Their Uptake and Subsequent Intracellular Growth.** *J. Bacteriology.* 1959, June, v. 77, No. 6, 701–14, 6 figs. [24 refs.]

Bacteria will only grow in tissue cells if the conditions obtaining allow the bacteria to gain entrance to the cell. Certain tissue cells normally phagocytose bacteria, but tissue culture systems, such as the human HeLa tissue culture cells, do not take up bacteria when the usual tissue culture media are employed. If, however, an appropriate serum medium is used bacteria can gain entrance to the cell itself and multiply within it.

The uptake by HeLa cells of different bacterial species was promoted selectively by sera of different animal species when the sera were incorporated in the tissue culture media in a concentration of 20%. Thus it was found that uptake of *Brucella tularensis* and *Salmonella typhi* were promoted by dog serum, group D streptococci by guineapig serum and *Brucella abortus, Br. melitensis* and *Br. suis* by chicken and guineapig sera. Tissue culture medium containing 20% of the appropriate serum was used to infect the cell but it was found that many of the bacteria studied were able to grow in the extracellular fluid so that if they were not taken up rapidly by the cells they multiplied and soon altered the condition of the tissue culture medium so that the HeLa cells suffered damage. If, however, the organism gained entrance to the cells the tissue culture medium could usually be changed to one containing 40% human serum and streptomycin; further phagocytosis would then be minimal, extracellular bacterial growth would be stopped and the tissue culture cells optimally nourished. Natural human pathogens grew in the cytoplasm of the tissue culture cells at rates related to their optimal growth on ordinary laboratory bacteriological media. Bacterial species of low or doubtful pathogenicity grew much more slowly when cells were successfully infected with such organisms.

[See also this *Bulletin*, 1958, v. 33, 609, 878.]

*H. J. Bensted*

POHUNEK, M., with the technical assistance of M. SKRUZNÁ. Bakteriologické nálezy na penězích. [**Bacteriological Findings on Money**] *Československ. Hyg.* Prague. 1959, v. 4, No. 9, 555–65, 5 graphs & 3 figs. [17 refs.]

The English summary appended to the paper is as follows:—

"The presence of aerobe microbes was determined on current money now in circulation as well as the time of their survival after the money has been withdrawn from circulation.

"There were investigated 1 crown bank-notes from paper money—a total of 345 samples—and 10 heller coins from metal money—458 pieces in all. A reproduction and copy method was used. It has been found that very few intestinal bacteria are present. The percentage of microbes with fixed plasma coagulase was about 18–43%.

"It has been revealed that on paper money the presence of bacteria rapidly decreases depending on the temperature and humidity of atmosphere. This phenomenon has not been confirmed on aluminium money.

"The findings suggest then that infection may be transmitted through the intermediary of money, especially in direct contact and in rapid circulation, but the transmission is not more likely in the case of money than with other objects of everyday use. Moreover, paper money that is considered as worst contaminated does not differ significantly from coins and more than that—it has shown surprising autosterilization properties."

WENDT, F. Neue Ergebnisse der Pyrogenforschung. Bakterielle Pyrogene. [**Recent Advances in Pyrogen Research: Bacterial Pyrogens**] *Deut. med. Woch.* 1959, Nov. 13, v. 84, No. 46, 2084–9. [Numerous refs.]

SMIRNOFF, W. A. **A Portable Heating Unit for Sterilizing Bacteriological Inoculation Loops.** *Canadian J. Microbiol.* Ottawa. 1959, Oct., v. 5, No. 5, 561–3, 2 figs.

## BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Other Therapeutic Substances; Disinfection.**

RYAN, W. L., IGEL, H. J. & WILLIAMS, P. T. **Simple Paper Test for determining Bacterial Sensitivity to Antibiotics.** *J. Amer. Med. Ass.* 1959, July 25, v. 170, No. 13, 1528–30, 2 figs.

The authors of this paper are respectively Assistant Professor of Biochemistry, a medical student, and Instructor in Medicine, at Creighton University School of Medicine, Omaha. Their cultures are made on an oblong piece of filter paper with 4 projections on each side: the paper is impregnated with tryptose phosphate broth containing 0·01% triphenyltetrazolium chloride and antibiotic solutions are pipetted on to the projections. The paper is then dried and kept until required. For use it is first floated on tap water, then "swabbed with the infectious material" and incubated in a plastic sack. Bacterial growth reduces the tetrazolium salt, producing a red colour: absence of this change on a projection containing an antibiotic indicates sensitivity. Results tallied with those obtained by a tube dilution or disk plate method, and treatment based on them was successful. [This is amateur bacteriology at its worst. Some important pathogens would not grow at all on this contrivance, and many indifferent bacteria would, producing a misleading result: materials cultivated in which a mixed pathogenic and non-pathogenic flora is to be expected include swabs from ear, nose and throat, and even faeces! The authors seem fortunate in having got helpful results from the method, and their recommendation that it be adopted for "general office practice" cannot conscientiously be endorsed.]

*L. P. Garrod*

OCKLITZ, H. W. & SCHMIDT, E. F. Stuhlflora-Analysen bei mit Antibiotika behandelten Säuglingen. [**Analysis of the Stool Flora of Infants treated with Antibiotics**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 402–23, 5 figs. [50 refs.]

This paper from the University Children's Clinic, Rostock, describes an extremely laborious and painstaking study of the faecal flora of infants on different diets and during the administration of various antibacterial drugs. A quantitative method of culture was used, and different special media were used for lactobacilli (separately enumerated as *L. acidophilus* and *L. bifidus*) *Escherichia coli,* staphylococci, streptococci, fungi (*i.e. Candida*) and *Proteus.* (There is no mention of clostridia or *Bacteroides.*) The results are presented in diagrams and graphs of great complexity.

The diets were natural breast milk, sterilized breast milk and 6 varieties of artificial feed, and some minor conclusions are drawn about the effects of these on various elements of the flora. The antibiotics, etc., were given for 7 or 14 days, and fluctuations in the numbers of the 7 named varieties of bacteria before, during and after this treatment are recorded as graphs. These (naturally) pursue somewhat irregular courses, and it sometimes seems difficult to decide whether changes are accidental or caused by the medication. Penicillin (50,000 units daily) seems to have been without effect except that it depressed the lactobacilli when given orally, and possibly *L. bifidus* only when given intramuscularly. Streptomycin (200 mgm.) depressed both varieties of lactobacilli, *E. coli* and streptococci. Chloramphenicol (80 mgm.) seems to have caused an increase in the numbers of streptococci and *Candida,* but no other definite change. Tetracycline (40 mgm.) depressed lactobacilli and staphylococci. Sulphaguanidine (300 mgm.) seems to have had little effect except an increase in streptococci. "Nebacetin" (neomycin and bacitracin, the daily dose being respectively about 80 mgm. and 6,000 units) had much the greatest effect, apparently depressing all the varieties of bacteria, some profoundly, only *Candida* being unaffected. Films of such faeces showed relatively few bacteria. These were always made, and rather poor photographs of 4 showing the effect of Nebacetin are reproduced. *L. P. Garrod*

DAIKOS, G. K. & ATHANASIADOU, Maria, with the technical assistance of P. KOUSKOUMVEKAKI. **Penicillin Sensitivity of Gram-Negative Enteric Bacilli. Successful Treatment of Urinary Tract Infections.** *Arch. Intern. Med.* 1959, Sept., v. 104, No. 3, 378–84. [11 refs.]

"The problem of the urinary tract infections that resist the usual chemotherapy is growing in importance every day. In an effort to tackle it, we set out testing Gram-negative organisms for sensitivity to high concentrations of penicillin." The methods of laboratory study employed by the authors of this paper are described and it was found that out of 250 strains of Gram-negative enteric bacteria isolated from clinical material and tested for sensitivity by the disk method (content of each disk, 60 μgm. of penicillin) 72 proved to be sensitive to penicillin in that high concentration. These sensitive strains were *Escherichia coli* (52), *Klebsiella pneumoniae* (13), *Proteus* species (5), and *Bact. alcaligenes* (2). Of these strains 31 were further examined for penicillinase production and to determine the exact minimal inhibitory concentration of penicillin which was found to range from 7·5 to 120·0 μgm. per ml. Penicillinase production was marked in only 7 strains. There is an analysis of 16 cases of Gram-negative infections by organisms proved sensitive to high concentrations of penicillin in which the patients were treated by large doses of penicillin. Some detailed case reports are given. In 13 patients with urinary infection penicillin treatment (intramuscular crystalline aqueous form) in doses ranging from 10,000,000 to 1,600,000 units daily had "dramatic effects". In 2 cases of pneumonia and 2 of gynaecological infection there was no favourable response to penicillin.

*M. E. Delafield*

BENVIGNATI, S. & AVANZINI, F. **The Pharmacology of α,β,Bis(paradimethylamido-sulphonobenzylamino)-ethane and of α,β,Bis(paradimethylamido-sulphonobenzylamino)-ethane · Dipenicillin G.** *Antibiotics & Chemotherapy.* New York. 1959, Sept., v. 9, No. 9, 557–61, 4 figs.

"The main chemical and pharmacological characteristics of α, β, bis(paradimethylamido-sulphonobenzylamino)-ethane and its dipenicillin salt are described. The dipenicillin salt is a repository penicillin salt possessing an extremely low toxicity."

SHAMBAUGH, G. E., Jr., DERLACKI, E. L., HARRISON, W. H., HOUSE, H., HOUSE, W., HILDYARD, V., SCHUKNECHT, H. & SHEA, J. J. **Dihydrostreptomycin Deafness.** *J. Amer. Med. Ass.* 1959, Aug. 1, v. 170, No. 14, 1657–60, 2 figs.

This is a report sponsored by the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otorhinolaryngology. It begins by pointing out, first that deafness produced by dihydrostreptomycin may develop as long as 6 months after its administration, and secondly that the alleged lesser toxicity of a mixture of streptomycin and dihydrostreptomycin has led to the inclusion of both in proprietary antibiotic mixtures bearing names not betraying their composition: these are often given in circumstances not meriting the use of a dangerous drug.

Particulars are given in a table of 32 cases of loss of hearing varying in degree but usually of considerable severity which followed the administration of dihydrostreptomycin, either alone or in mixtures with other antibiotics, in total doses which in 18 cases did not exceed 10 gm. The diagnosis in 6 was tuberculosis, but most of the remainder seem to afford little indication of the necessity for such treatment (*e.g.* influenza, cold, asthma, boils, mononucleosis, encephalitis). In 3 women (one a telephone operator aged 39) the antibiotic was given prophylactically after hysterectomy, and in 3 other patients after appendectomy: 4 cases of urinary tract infection are included in a miscellany of other diagnoses. Only 6 were over 60 years of age: nothing is said about impairment of renal function.

The authors conclude that dihydrostreptomycin "should be omitted from commercial combinations of antibiotics, or if included its presence should be clearly indicated in the name". (The existing names of incriminated combinations are Combiotic, Dicrysticin, Districillin, Strocillin and Durycin.) *L. P. Garrod*

SUTHERLAND, J. M. **Fatal Cardiovascular Collapse of Infants receiving Large Amounts of Chloramphenicol.** *J. Dis. Children.* Chicago. 1959, June, v. 97, No. 6, 761–7. [52 refs.]

This paper gives the case histories of 3 infants who died 7, 4 and 7 days after birth after the administration of chloramphenicol in doses exceeding those recommended. The first child was at first given procaine penicillin and streptomycin because of premature rupture of the membranes during labour, but on account of signs of umbilical sepsis on the third day he was given 250 mgm. chloramphenicol every 8 hours by intramuscular injection: 8 doses in all were given. The second child was treated with antibiotics because of "meconium staining" and a "foul odor": he received 9 × 250 mgm. doses of chloramphenicol at 8-hour intervals, together with procaine penicillin. The third child was delivered by Caesarian section, and was given at first procaine penicillin and streptomycin, and next 50 mgm. of chloramphenicol palmitate every 8 hours for 7 doses, then a single dose of 400 mgm. [apparently in error], the indication for treatment being "abdominal distension". Each infant suffered cardiovascular collapse and died within a few hours.

Post mortem examination in each revealed neither an immediate cause for death, nor apparently any signs of the supposed infections for which the treatment had been given. A few previous reports of collapse following treatment with this antibiotic are discussed.

[The paper does not reveal why such large doses were given to patients 1 and 2, or why this antibiotic was chosen, nor does it discuss the advisability of giving antibiotics at all for such vague indications, with no information about the nature of the infection, in any.]

*L. P. Garrod*

WEGMANN, T. & BELSER, F. Klinische Erfahrungen mit einem intravenösen Tetrazyklin (Reverin). **[Clinical Experience of Intravenous Administration of Reverin, a Tetracycline]** *Schweiz. med. Woch.* 1959, Sept. 12, v. 89, No. 37, 962–5, 3 figs. [13 refs.]

Reverin is the trade name (Plüss-Staufer A.G., Zürich) given to pyrrolidinomethyltetracycline which has a water solubility of 1,250 mgm. per 1·0 ml. (2,500 times that of tetracycline) and can therefore be administered intravenously. The characters of Reverin are similar to those of tetracycline in respect of toxicity for experimental animals and bacteriostatic action. Experiments on the concentration of Reverin in blood serum after intravenous injection have given satisfactory results. The clinical experience of intravenous Reverin in 109 patients with infections of the urinary and respiratory systems, of the skin and biliary passages and other organs is described and tabulated. Some case histories are given. The conclusion is that Reverin has the same clinical effect and bacteriological spectrum as tetracycline hydrochloride but in addition is well tolerated and has practically no side effects. *M. E. Delafield*

MILLER, A. Kathrine, VALIANT, Mary E. & FROST, Bettina M., with the technical assistance of D. G. KELLER. **Laboratory Studies on the Antibacterial Activity of Kanamycin.** *Antibiotics & Chemotherapy.* New York. 1959, Aug., v. 9, No. 8, 475–84, 4 figs. [11 refs.]

This paper from the Merck Institute for Therapeutic Research describes a comparison of kanamycin with neomycin, and in some experiments with streptomycin. The bacteriostatic activity of neomycin against 33 strains of 16 species of bacteria was found to be in general somewhat greater than that of kanamycin, but the only

wide differences were against some strains of *Pseudomonas pyocyanea*: the only differences in favour of kanamycin were against *Pasteurella multocida* and 2 strains of *Proteus vulgaris*. The addition of 10% serum had little effect on the action of either. Both were bactericidal in about 4 times the bacteriostatic concentration. Mg ++ as magnesium sulphate reduced the activity of both. Resistance to each developed in *Escherichia coli* and *Staphylococcus aureus* at about an equal rate, and much more slowly than to streptomycin; there was cross-resistance between neomycin and kanamycin, but little between either of these and streptomycin. Therapeutic tests in mice infected with 7 species of bacteria showed the protective dose of neomycin to be usually lower than that of kanamycin when given subcutaneously, but that of kanamycin was sometimes lower than that of neomycin by the oral route, kanamycin being apparently better absorbed from the mouse alimentary tract (the effective oral doses of both were of course much larger than the subcutaneous). The greatest difference in therapeutic efficacy was in *Ps. pyocyanea* infection, kanamycin being decidedly inferior. [The authors do not say which of the strains tested *in vitro* were used in therapeutic tests. Much might depend on this, since the relative activities of the 2 antibiotics against different strains of *Ps. pyocyanea* varied widely, and to a lesser extent against those of *P. vulgaris*.] *L. P. Garrod*

Finegold, S. M. **Kanamycin.** *Arch. Intern. Med.* 1959, July, v. 104, No. 1, 15–28, 2 figs. [58 refs.]

This is a useful review on the literature on kanamycin, which is already considerable, although this antibiotic was first described in Japan only 2 years ago. It gives the structural formula of kanamycin, details its antibacterial spectrum, discusses its relationships with other antibiotics (those with neomycin and paromomycin being very close) and gives particulars of its absorption, distribution and excretion.

Therapeutic use is divided into oral, with the object of suppressing the bowel flora for various purposes, and parenteral, the chief indications for which are Gram-negative infections (*Escherichia, Salmonella,* particularly *Proteus,* and others), some staphylococcal infections, and perhaps otherwise chemo-resistant tuberculosis, particularly if it should prove satisfactory to give a dose only 2 or 3 times a week.

Damage to the eighth nerve, usually the auditory branch, is the chief danger: evidence is adduced that a daily dose of over 15 mgm./kgm. is much more likely to cause this, but it is uncertain whether the total dose given in a course is also a factor. Daily questioning about tinnitus and serial audiograms are suggested in order to detect damage at the earliest stage: owing to the greatly aggravating effect of impaired renal function, blood urea estimations should be done 3 times a week. These and other precautions are detailed in an appendix.

[The author does not venture an opinion on whether kanamycin is less toxic than neomycin, which if true would be its only important advantage, since the therapeutic activity of these 2 antibiotics is almost identical.] *L. P. Garrod*

Ozeki, H., Stocker, B. A. D. & De Margerie, Helène. **Production of Colicine by Single Bacteria.** *Nature.* 1959, Aug. 1, v. 184, 337–9.

The authors have demonstrated that a colicine liberated by a bacterial culture is formed by only a fraction of the cells of the culture, and that this fraction is not viable. This has been shown (1) by investigating the conditions in which clear spots or "lacunae" are produced by colicine E2 released from *Salmonella typhimurium* LT2 on a layer of cells of *Escherichia coli* strain $\phi$ which is sensitive to colicine E2, and (2) by analysing the production of the colicine by single cells of *Salm. typhimurium,* isolated by micromanipulation.

Lacunae, observed in a soft agar overlayer, appeared only when cells of the colicinogenic strain were plated with cells of a sensitive strain. They looked like phage plaques, but were not transmissible. No lacunae developed if the cultures were plated in the presence of trypsin, which destroys colicine. The number of lacunae was proportional to the number of salmonella cells and was not changed by killing the cells with chloroform before plating. 10–100-fold fewer lacunae were seen when the salmonella strain (sensitive to streptomycin) and the indicator (resistant to streptomycin) were plated in the presence of streptomycin, which suggested that most lacunae were made by colicine synthesized during bacterial growth on the plate, but that some were produced by cells which, at the time of plating, already contained enough colicine to make a lacuna. When the salmonellae were first grown in the presence of trypsin, and then plated on a medium containing streptomycin and trypsin-inhibitor, the number of lacunae was unchanged, indicating that lacunae could not be formed by cells adsorbing colicine and releasing it later. UV-irradiation of the colicinogenic strain increased the number of lacunae produced. With a dose of UV which reduced bacterial viability to 30%, at least half of the total number of bacteria counted gave rise to lacunae.

Under the microscope, the colicinogenic cells of *Salm. typhimurium* were short and motile, and easily distinguished from the non-motile filaments of the indicator strain. When a culture of *Salm. typhimurium* was grown in the presence of trypsin to destroy free colicine, exposed to UV light, and single cells isolated from it and incubated for 2 hours in broth containing trypsin-inhibitor, only 20% of the cells multiplied, although the remainder were still visible. When cells of the indicator strain were added, it was found that in those micro-drops in which multiplication of the indicator cells was inhibited no multiplication of the colicinogenic strain had occurred. After irradiation about 50% of the individual cells tested released colicine, which agreed with the finding that 6 out of 10 bacteria produced lacunae.

The fact that the cells producing colicine were not viable was confirmed with unirradiated cultures. It was observed that, in conditions favouring their growth, no colonies developed at the centre of lacunae, presumably because the bacteria which produced the clearings by releasing colicine were themselves unable to multiply. *Janice Taverne*

VAN DIJCK, P., CLAESEN, M., VANDERHAEGHE, H. & DE SOMER, P. **Pyrimidines. VII. Chemotherapeutic Properties of Hydrazinopyrimidines.** *Antibiotics & Chemotherapy.* New York. 1959, Sept., v. 9, No. 9, 523–9. [10 refs.]

"The study of a number of condensation products of hydrazinopyrimidines with various aromatic and heterocyclic aldehydes and ketones revealed a structure essential for tuberculostatic activity. Several products were active against a wide range of fungi."

DAWSON, F. W., HEARN, H. J. & HOFFMAN, R. K. **Virucidal Activity of β-Propiolactone Vapor. I. Effect of β-Propiolactone Vapor on Venezuelan Equine Encephalomyelitis Virus.** *Applied Microbiol.* Baltimore. 1959, July, v. 7, No. 4, 199–201.

Venezuelan equine encephalomyelitis virus in the form of chick embryo suspension, both moist and dried, was inactivated in 15 minutes in an atmosphere containing 2 mgm. β-propiolactone per litre, with a humidity of 90% and at a temperature of 26°C. These findings suggest that beta-propiolactone "might be used as a replacement for formaldehyde as a gaseous disinfectant for the routine decontamination of large enclosed areas contaminated with viruses".

*L. P. Garrod*

ALBRECHT, J. Untersuchungen über die chemische Inaktivierung von Encephalomyocarditis- und Herpesviren. **[On the Chemical Inactivation of Encephalomyocarditis and Herpes Viruses]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 5/6, 333–43. [11 refs.]

Mouse brain suspension containing herpes or encephalomyocarditis (EMC) virus, with or without added brain suspension or serum to act as "ballast material" (*i.e.* interfering organic matter) was mixed with an equal volume of disinfectant solution, either in a single or several different concentrations, and kept at room temperature for 30 minutes. Serial dilutions were then made and mice were inoculated with these. Most of the paper consists of detailed tables of results with 18 disinfectants, 13 being pure reagents and 5 proprietary, the exact composition of which is stated. Some of the noteworthy features in these are the high efficacy of β-propiolactone against both viruses, the efficacy of formaldehyde and halogens provided not too much organic matter is present, the efficacy of phenol, *p*-chlor-*m*-cresol and hexylresorcinol against EMC but not against herpes virus, and an opposite difference in the action of Merthiolate, herpes virus being inactivated and EMC not. Other substances tested were other organic mercury compounds, acids, alkali and triethylene glycol (tested against EMC virus only and found ineffective).

*L. P. Garrod*

BECKETT, A. H.; PATKI, S. J.; ROBINSON, Ann E. **The Interaction of Phenolic Compounds with Bacteria. Part I. Hexylresorcinol and** *Escherichia Coli.* [BECKETT, PATKI & ROBINSON]. *J. Pharmacy & Pharmacol.* London. 1959, June, v. 11, No. 6, 360–66, 3 figs. [18 refs.] **Part II. The Effects of Various Substances on the Interaction of Hexylresorcinol with** *Escherichia Coli.* [BECKETT, PATKI & ROBINSON]. *Ibid.*, 367–73, 4 figs. [12 refs.]

A paper by the same authors immediately preceding these describes methods for extracting hexylresorcinol and other antibacterial substances from solutions added to bacterial suspensions and assaying them spectrophotometrically. The object is to determine how much of these substances is bound to the bacteria on which they act under different conditions; results of such determinations are reported here. When hexylresorcinol solution was added to a suspension of *Escherichia coli*, its uptake by the organism was rapid: it was shown to be greater the greater the concentration of hexylresorcinol between the limits of 20 and 440 μgm./ml. It was also affected by temperature, but to a much smaller extent. Only 6% of the amount bound by whole bacteria was bound by a corresponding quantity of separated cell walls: for this and other reasons it is concluded that the germicide must enter the cell and does not merely act on its surface. Determinations were also made by a spectrophotometric method of the amount of "cell exudate" released during hexylresorcinol treatment (*i.e.* cellular constituents escaping owing to damage to the cell).

The second paper records similar observations on the action of hexylresorcinol on heat-killed and butanol-treated bacteria, and on its action in the presence of cetomacrogol and of sodium chloride, which respectively reduce and enhance the bactericidal action. Cetomacrogol, a non-ionic surface-active agent, greatly reduced the uptake of hexylresorcinol: sodium chloride slightly enhanced it, and caused a much greater increase in the amount of cell exudate liberated. A further paper in the same journal (1959, v. 11, 421) describes experiments of the same kind and speculates on their significance.

*L. P. Garrod*

FRISBY, B. R. **"Tego" Compounds in Hospital Practice.** *Lancet.* 1959, July 25, 57–8.

Tego compounds are "amino acids of high molecular weight and are ampholytic surface-active bactericidal agents": 3 different compounds, the chemical composition of which is stated, were used in these tests. Tegolan Emulsion was used for the disinfection of the skin before putting on gloves: the skin was swabbed before this treatment, and again after the gloves had been worn for at least an hour, by pushing a swab between the glove and the palm of the hand and into a finger. These swabs were cultivated in meat broth which was later plated. Tego 103S was used for the pre-operative disinfection of the patient's skin, and swabs were taken before this process and at the end of the operation. Results are stated as numbers of cultures yielding no growth and numbers yielding various bacteria. The great majority of the second swabs in both series were sterile [but the fact that 3 out of 51 in the first series and 5 out of 24 in the second were sterile *before* the treatment was applied suggests that the method was faulty].

Finally Tego MHG, sprayed with a machine, was used for disinfecting the floors and walls of an operating theatre and adjoining rooms, and the floors of wards, and similar rather fragmentary information is given about the effects as judged by swabbing before and during the period of application of this process. The 2 organisms looked for in these cultures were *Staphylococcus aureus* and *Clostridium welchii*, and it appears to be claimed that both were eliminated, at least from the theatre: treatment of boots which were believed to be carrying *Cl. welchii* into the theatre also removed this organism from them. [No general information about the bactericidal properties of this class of compound is given. If it is a fact that these compounds will kill spores of clostridia, this is sufficiently remarkable to deserve explicit affirmation.]

*L. P. Garrod*

MORTLOCK, Nita J. & DAVIS, J. G. **The Influence of Methods of Sterilisation on the Bacteriological Quality of Babies' Napkins.** *Med. Officer.* 1959, Oct. 23, v. 102, No. 17, 210–13.

Two chemical agents were compared with boiling for their efficiency as terminal disinfectants of soiled babies' napkins. The chemicals were Napisan A, in which lauryl-dimethyl-benzyl-ammonium chloride was the active substance, and Napisan B which contained in addition a soluble cresol. Both formulations were used to prepare a weak solution into which soiled napkins were discarded during the day and in which they were soaked until being washed the following morning. Preliminary suspension tests with *Escherichia coli* type 1, *Brevibacterium ammoniagenes* and *Salmonella bovis-morbificans* showed that Napisan A at a concentration of one-third of an ounce per gallon killed 99·999% of all these organisms in a 5-minute contact time. The working concentration was half-an ounce per gallon.

In a field trial, washed napkins ready for use were collected weekly in sterile containers from 13 mothers and examined by rinsing in 800 ml. of Ringer's solution, after which plate counts at 30°C. for 4 days in Yeastrel milk agar and presumptive coliform counts were done on the rinse. In later experiments, the rinse was plated on to urea agar to detect urea splitting organisms. The trial consisted of 4 periods (of unspecified duration) during 2 of which the mothers used their own boiling routine. These periods alternated with periods in which Napisan A and B were used respectively, without boiling.

The average counts for the boiled napkins ranged from 764,894 to 22 per ml. of rinse, those from the chemically disinfected napkins ranged from 58,921 to 9. In general, counts from the latter were rather lower and the same "order of merit" as between different mothers was observed. The presumptive coliform test was positive in 32% of boiled napkins, 22% of those disinfected with Napisan A and 5% with Napisan B. During the control periods, there were 4 cases of napkin rash—there were none during the periods of chemical disinfection.

The authors conclude that Napisan B is to be preferred in view of its greater reduction of the coliform count, and that the use of either formulation was at least equally effective as boiling. They record as a matter of general interest that they observed a clear correlation between bacterial count and home conditions. They also noted a pure growth of *Staphylococcus aureus* over a period from the napkins from a family where there had been a history of food poisoning.

[The high counts that can be obtained from *boiled* napkins are notable and probably reflect unhygienic handling and storage rather than inadequate heat treatment.]

*J. C. Kelsey*

OPPENHEIMER, F., BENESI, E. & TAYLOR, A. R. **The Ultraviolet Irradiation of Biological Fluids in Thin-Flowing Films.** *Amer. J. Pub. Health.* 1959, July, v. 49, No. 7, 903–23, 10 figs. [40 refs.]

This paper is chiefly of engineering interest, since it describes and illustrates in full detail a machine known as the Centrifilmer, which enables very thin films of various fluids to be exposed to bactericidal ultraviolet light irradiation. The core of this is the "bowl", actually a stainless steel cylinder, 16 inches long and tapering slightly from top to bottom. This rotates at high speed, and fluid admitted at the bottom forms a film on the inner wall dependent on the flow rate and other factors, including viscosity (a graph showing this relationship covers the range of film thickness 0–140$\mu$). A source of suitable irradiation is mounted centrally in the bowl. The fluid flows continuously upward and is drained off from the top, the rate of flow being about 35 litres per hour.

This machine is designed for the sterilization of serum or plasma, and for the inactivation of virus vaccines etc. It is mentioned that rabies virus is very sensitive to light and can satisfactorily be treated by this means alone, whereas poliomyelitis virus requires a more damaging dose and is best treated by a combination of irradiation and formalin.

*L. P. Garrod*

BEEBE, J. M. **Stability of Disseminated Aerosols of *Pasteurella tularensis* subjected to Simulated Solar Radiations at Various Humidities.** *J. Bacteriology.* 1959, July, v. 78, No. 1, 18–24, 3 figs.

Clouds of *Brucella tularensis* were dispersed into a 20-litre chamber which could be held at desired humidities, and exposed to simulated solar radiation. The cloud was sampled at intervals and the "minute decay rate" calculated. When a liquid suspension was sprayed, without irradiation, the maximum decay rate was at R.H. 60%; under irradiation the maximum was greatly increased and was at R.H. 25%, and increasing humidity progressively decreased the decay. When dried culture was dispersed into the chamber, the maximum death rate was at about R.H. 60%, with or without irradiation; the bactericidal action was nevertheless roughly proportional to the light intensity.

*R. E. O. Williams*

## BACTERIA

The order in this section:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

ESBER, R. J. & FAULCONER, R. J. **A Medium for Initial Visual Demonstration of Production of Coagulase and Fermentation of Mannitol by Pathogenic Staphylococci.** *Amer. J. Clin. Path.* 1959, Aug., v. 32, No. 2, 192–4.

A medium is described which contains mannitol, an indicator and 7% human plasma, and which permits the identification of pathogenic staphylococci in 12–24 hours. The medium is clear purple-blue and mannitol-fermenting coagulase-positive staphylococci become surrounded by a yellow opaque halo. Their colonial morphology distinguishes them from the few strains of *Escherichia coli* which produce coagulase and ferment mannitol.

The medium permits the growth of fastidious organisms as well as the detection of pathogenic staphylococci. It is easy to prepare and keeps for up to 6 months. *M. Patricia Jevons*

OEHRING, H. Die Verwendung des *Bacterium anitratum* zum Nachweis der Hyaluronidase bei Staphylokokken. [**The Use of *Bacterium anitratum* for the Demonstration of Hyaluronidase in Staphylococci**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 176, Nos. 1/2, 59–65. [12 refs.]

Cultures of *Bacterium antitratum* were used to demonstrate hyaluronidase production by staphylococci, with the use of the cross-culture method. 457 strains of staphylococci were tested for hyaluronidase, coagulase and plasma clumping; the numbers giving positive reactions in the 3 tests were, respectively, 219, 199 and 222. *R. E. O. Williams*

STEFANESCO, V., MANOLIU, N., BRAILOIU, A. & BUSTEA, C. Une nouvelle méthode de détermination du caractère de pathogénité des souches de staphylocoque sur l'animal. [**A New Method for the determination of the Pathogenic Character of *Staphylococcus* Strains in Animals**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Mar., v. 18, No. 1, 77–81.

0·2 ml. of an overnight broth culture of the staphylococcus under test is inoculated into the pleural cavity of mice. With pathogenic strains most mice die within 24 hours, apparently from toxaemia. Injection of the culture into the lung kills the mice in 2–3 minutes and such deaths are excluded from the calculations. "Non-pathogenic" strains do not kill the mice.

*R. E. O. Williams*

WILSON, B. J. **Comparative Susceptibility of Chimpanzees and *Macaca mulatta* Monkeys to Oral Administration of Partially Purified Staphylococcal Enterotoxin.** *J. Bacteriology.* 1959, Aug., v. 78, No. 2, 240–42.

*Macaca mulatta* monkeys were given partially purified staphylococcal enterotoxin orally. 5 out of 5 monkeys were symptomless after a dose of 0·125 mgm. but 11 out of 19 showed toxic symptoms after 0·250 mgm.

Toxin was then given in a banana to each of 5 chimpanzees. The 2 animals receiving 0·0017 mgm./kgm. body weight were asymptomatic during the 2-day observation period. The animal receiving 0·0022 mgm./kgm. body weight had mild diarrhoea starting after 18 hours and lasting about 24 hours. The 2 animals receiving between 0·01 and 0·02 mgm./kgm. body weight showed symptoms in 1 to 2 hours and vomited profusely at 2 hours for about 2 hours. Diarrhoea began the next day and continued 1½ days; appetite recovered over the next 2 days.

Similar experiments in *Macaca mulatta* monkeys showed that they were 10 times less susceptible to the toxin than chimpanzees. *M. Patricia Jevons*

KUKULSKA-GOSCICKA, T., MICHNA-BEDNAREK, Z. & ZABŁOCKI, B. **Variation of *Staphylococcus aureus* Strains grown on Isolated Mouse Organs.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 10, 405–8.

WOODIN, A. M. **Fractionation of a Leucocidin from *Staphylococcus aureus*.** *Biochem. J.* 1959, Oct., v. 73, No. 2, 225–37, 10 figs. [16 refs.]

STROMINGER, J. L. & THRENN, R. H. **Accumulation of a Uridine Nucleotide in *Staphylococcus aureus* as the Consequence of Lysine Deprivation.** *Biochim. et Biophys. Acta.* 1959, Nov., v. 36, No. 1, 83–92, 6 figs. [30 refs.]

FUSILLO, M. H. & WEISS, D. L. **Qualitative Estimation of Staphylococcal Deoxyribonuclease.** *J. Bacteriology.* 1959, Oct., v. 78, No. 4, 520–22.

RICHMOND, M. H. **Incorporation of Canavanine by *Staphylococcus aureus* 524 SC.** *Biochem. J.* 1959, Oct., v. 73, No. 2, 261–4. [25 refs.]

FUSILLO, M. H. & WEISS, D. L. **Selection of Antibiotic-Sensitive Staphylococci from Antibiotic-Resistant Populations by 2,4-Dinitrophenol and Sodium Salicylate.** *Antibiotics & Chemotherapy.* New York. 1959, Aug., v. 9, No. 8, 455–8.

Reasons are first advanced for supposing that substances interfering with oxidative phosphorylation may

deprive staphylococci of antibiotic resistance [this *Bulletin*, 1958, v. 33, 685]. Strains resistant to penicillin, streptomycin and tetracycline were cultivated in broth containing falling (from 0·25%) dilutions of 2,4-dinitrophenol and plated: many colonies were then tested for antibiotic sensitivity. Many were found to be sensitive to penicillin and smaller numbers to all 3 antibiotics [criteria of sensitivity are not defined, although degrees of original resistance are specified]. Similar experiments with sodium salicylate, in dilutions falling from 1%, yielded organisms sensitive to penicillin or tetracycline or both but not to streptomycin.

*L. P. Garrod*

Ehrenkranz, N. J. & Rommel, F. A. **Influence of Sodium Chloride on Antibiotic Action against Coagulase-Positive and Coagulase-Negative Staphylococci.** *Antibiotics & Chemotherapy.* New York. 1959, Aug., v. 9, No. 8, 459–63, 2 figs.

In view of the possibility that antibiotics may be added to brine agar used for the isolation of staphylococci it is advisable to know what effects this medium may have on antibiotic action. Plates containing 3 different concentrations of antibiotic and either 0·5 or 7·5% of sodium chloride were inoculated in an unusual way (with an instrument "consisting of 40 to 50 sterile pins in a wooden base") with 11 strains of coagulase-positive staphylococci. The higher concentration of sodium chloride enhanced the action of novobiocin and chloramphenicol but not that of penicillin, erythromycin or tetracycline. Coagulase-negative staphylococci were also more sensitive to novobiocin and chloramphenicol in the brine medium, but sometimes less sensitive in it to the other 3 antibiotics.

*L. P. Garrod*

i. Meyer, J., Malgras, J. & Viguié, J. J. Influence de l'acide pantothénique sur l'évolution de l'immunité antistaphylococcique. [**The Influence of Pantothenic Acid on Immunity to Staphylococci**] *Rev. d'Immunologie.* 1958, Oct.–Dec., v. 22, Nos. 5/6, 522–5.

ii. ——, —— & ——. Influence de l'acide pantothénique sur l'état d'hyperimmunisation. [**The Influence of Pantothenic Acid on Hyperimmunization**] *Ibid.*, 526–9.

i. The authors immunized rabbits with either staphylococcal toxoid or vaccine, by subcutaneous and increasing doses at intervals of 4 days on 4 occasions, and injected 0·1 cc. of pantothenic acid on each occasion and once after the end of the course. An increase in the beta and gamma globulins was observed.

ii. In later work the authors doubled the amount of pantothenic acid to 0·2 cc., and observed an acceleration of production of increased amounts of beta and gamma globulin.

*Charles Wilcocks*

Richou, R. & Richou, H. Acide pantothénique et immunité antistaphylococcique. [**Pantothenic Acid and Antistaphylococcal Immunity**] *Rev. d'Immunologie.* 1959, Apr.–June, v. 23, No. 3, 127–32. [Refs. in footnotes.]

Injection of pantothenic acid into rabbits during a course of immunization with staphylococcal toxoid could not be shown to affect antitoxin production, or the stability of the serum titre over a period.

*R. E. O. Williams*

Richou, R. & Richou, H. Comparaison entre l'immunité spécifique obtenue chez des lapins, préalablement immunisés, ayant reçu une ou plusieurs injections de rappel d'anatoxine staphylococcique, additionnée ou non d'hydroxyde d'aluminium. [**Comparison between the Specific Immunity obtained in Rabbits, Previously Immunized, after one or more Recall Injections of Staphylococcal Toxoid with or without Aluminium Hydroxide**] *Rev. d'Immunologie.* 1959, Apr.–June, v. 23, No. 3, 123–6.

The addition of aluminium hydroxide to staphylococcal toxoid did not reduce its effectiveness as a recall injection in raising the antitoxin level in immunized rabbits, as has been claimed for diphtheria and tetanus toxoid [see also this *Bulletin*, 1957, v. 32, 631].

*R. E. O. Williams*

Neter, E., Gorzynski, E. A., Drislane, A. M., Harris, A. H. & Rajnovich, E. **Detection of Staphylococcal Antibodies in Human Gamma Globulin and Serum by Hemagglutination Tests.** *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 484–7. [17 refs.]

The haemagglutination test and 2 modifications of it were used in the detection of staphylococcal antibodies in human serum and gamma globulin.

The growth from 18-hour cultures of strains of *Staph. aureus, Staph. citreus* and *Bacillus subtilis* was washed off in buffer, spun and the supernatants used as antigens. These were added in suitable dilutions to washed group O human cells. The mixture was incubated at 37°C. for 30 minutes and washed. These modified cells were added to gamma globulin or serum dilutions, incubated at 37°C. for 30 minutes and lightly centrifuged. This formed the basic haemagglutination test.

The modified cells were incubated with pancreatic protease for the enzyme haemagglutination test. After enzyme treatment the cells were washed and added to serum dilutions as before.

For the Coombs haemagglutination test modified cells and serum dilutions were incubated as for the basic test, Coombs antiserum was then added and the mixture incubated, centrifuged and read as before.

The antigens from *Staph. citreus* produced no agglutination but those from 3 *Staph. aureus* strains produced varying amounts of agglutination, higher when tested with gamma globulin than with pooled human serum. Antibody titres of gamma globulin were considerably higher in the protease and Coombs haemagglutination test than in the basic test.

Gamma globulin absorbed by suspensions of *Staph. aureus* and *B. subtilis* failed to cause agglutination of red cells modified by either *Staph. aureus* or *B. subtilis*. *Staph. citreus* and several *Escherichia coli* strains failed to do this.

Possible reasons for the increased sensitivity of the two modifications of the basic test are discussed and the authors suggest that the antigen used in these tests is the

NSS antigen of RANTZ *et al.* [this *Bulletin*, 1956, v. 31, 1278]. *M. Patricia Jevons*

DOSSENA, G. Sull'isolamento e sulla tipizzazione degli streptococchi beta-emolitici. **[Isolation and Typing of Beta-Haemolytic Streptococci]** *Ann. Sclavo.* Siena. 1959, July–Aug., v. 1, No. 4, 431–40. [11 refs.] English summary (6 lines).

After a brief exposition of the various streptococcal types, the author describes the method he follows in typing beta-haemolytic streptococci. The swab by which the material has been taken is placed in a tube of azide blood agar (supplied by the Baltimore Biological Laboratory) in which it is incubated at 37°C. for 14–16 hours. The swab is then shaken in 5 ml. nutrient broth. Four plates of azide agar and 5% defibrinated rabbit blood are then inoculated. Colonies are picked and inoculated in liver broth. After 14–15 hours at 37°C. a mass of growth collects at the bottom of the tube. It is shaken up and then centrifuged at 3,000 r.p.m. for 10 minutes. The supernatant is removed and 0·5 ml. of N/5 hydrochloric acid is added. This is put in a water bath at 100°C. for 10 minutes. After neutralization with 0·5 ml. of N/5 sodium hydroxide it is centrifuged again, the supernatant now containing the antigen. Final *p*H should be between 6 and 7·5. A precipitation reaction is now carried out in capillary tubes against specific sera.

From 383 ill persons, 109 beta-haemolytic streptococci were isolated, of which 78 belonged to group A, 11 to group B, 2 to group C, and 18 to group G. From 55 healthy children 12 strains were isolated, 7 of group A, 2 of group C, and 3 of group G. *E. Agius*

GINSBERG, I. **Action of Streptococcal Haemolysins and Proteolytic Enzymes on Ehrlich Ascites Tumour Cells.** *Brit. J. Exper. Path.* 1959, Oct., v. 40, No. 5, 417–23, 9 figs. on 2 pls. [17 refs.]

MARUYAMA, Y., SUGAI, S. & EGAMI, F. **Formation of Streptolysin *S* by Streptococcal Protoplasts.** [Correspondence.] *Nature.* 1959, Sept. 12, v. 184, Suppl. No. 11, 832–3.

DEACON, W. E., PEACOCK, W. L., Jr., FREEMAN, Elizabeth M. & HARRIS, A. **Identification of** *Neisseria gonorrhoeae* **by means of Fluorescent Antibodies.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 322–5, 3 figs. [11 refs.]

This article is so technical and contains so much detail that an adequate abstract in a few words is not possible. Cultures and smears of numerous strains of gonococci were obtained and suspensions of the former killed by heating at 100°C. for 30 minutes, 120°C. for 2¼ hours and with 3% formalin for 30 minutes; antisera were prepared by injecting rabbits with these.

Agglutination experiments showed that gonococci may be inagglutinable in homologous antisera and that formalin preserved the "factor" responsible for this.

In a table are set out fluorescent antibody reactions obtained by staining various gonococci with absorbed and unabsorbed gonococcal antiserum labelled with fluorescein and typical fluorescent reactions are shown in 3 figures.

It is concluded that there is a species-specific antigen associated with freshly isolated inagglutinable gonococcus cultures; it appears to possess characteristics similar to Vi antigen of *Salmonella typhi* or the K antigens of the *Escherichia* group. Antisera containing GC-K(B) antibodies may be labelled with fluorescein and used to identify gonococci in smears. *T. E. Osmond*

SANI, A. Sui vantaggi dell'uso del terreno di cultura I.U.T.M. nell'isolamento del bacillo di Koch dall'espettorato, e nella ricerca della sensibilità ai chemioantibiotici antitubercolari. **[On the Advantages of ITU Medium for the Isolation of the Tubercle Bacillus from Sputum and for the Determination of Antibiotic Resistance]** *Ann. Sclavo.* Siena. 1959, Ju.y–Aug., v. 1, No. 4, 385–94. [10 refs.] English summary (6 lines).

A comparative study was made of the cultural efficiency of Petragnani's medium and of the medium proposed by the International Tuberculosis Union [the reader being referred to the original publications for details of the media] by culturing 22 sputa which microscopy after concentration had shown to be positive. Growth was obtained from 18 on Petragnani medium and from 20 on ITU medium; while growth was evident on ITU medium by the third week in all cases, in 10 of those which grew on Petragnani's medium, growth was delayed up to the fourth to the sixth week. From 142 sputa which were microscopically negative after concentration, positive cultures were obtained on both media in 12 cases, while 10 more were only positive on ITU medium and 2 only on Petragnani. 17 of the positives on ITU medium were so by the fifth week, but only 5 of those positive on Petragnani were so by that time. In no case was growth earlier on Petragnani than on ITU medium.

Resistance was found as follows in 19 strains examined:—Streptomycin 11 on ITU, 4 on Petragnani; isoniazid 10 on ITU, 2 on Petragnani; PAS 8 on ITU, 3 on Petragnani. Contaminants appear to be rare on ITU. *E. Agius*

COLETSOS, P. J., with the technical collaboration of E. ORIOT, N. de REGEL & M. G. MACHAVOINE. Étude des facteurs extrinsèques de "*Mycobacterium tuberculosis*" rendant aléatoire sa culture "*in vitro*". **[Extrinsic Factors counteracting the Culture of** *Myco. tuberculosis***]** *Ann. Inst. Pasteur.* 1959, Aug., v. 97, No. 2, 135–47, 2 figs. [16 refs.]

Tubercle bacilli are not infrequently seen in smears from pathological specimens from which few or no bacilli are grown. In this paper the author discusses the possible extrinsic causes of the paucity of growth and in his next paper he intends to discuss the intrinsic causes.

Treatment of the specimen with 4% solutions of NaOH, $H_2SO_4$ or HCl for homogenization, even when limited to 30 minutes, may reduce the number of viable organisms to less than 20%. Incorporation of antibiotics, *e.g.* penicillin, chloramphenicol or erythromycin, may also have an inhibiting effect, especially in liquid media; surface-active agents, *e.g.* Tween 80, Triton,

Span 20 and 80 also appear to reduce the growth from small inocula. Centrifugation at 3,000 r.p.m. for 60 minutes in uncooled centrifuges may destroy 70% of the bacilli, and at 7,000 r.p.m. the percentage destroyed may be 99·9%.

Saline is much more deleterious to tubercle bacilli than is pure distilled water, and neutralization after treatment with NaOH should be with $H_2SO_4$ and not HCl. Bronchial mucus has a protective action, but exposure of the bacilli to gastric juices, urine and caseous material reduces their viability. Experiments with lungs of tuberculous guineapig and with suspensions of bacilli suggest that the exposure to anaesthetics during resection reduces the number of recoverable bacilli.

The author summarizes the discussion by recommending that:—(1) chemotherapy be stopped for 3 days before collecting pathological specimens for the cultivation of tubercle bacilli (8 days in the case of urine specimens); (2) when the specimens are not treated immediately, they be kept at 4°C. but not for longer than 48 hours; (3) saline should not be used; (4) treatment with homogenizing agents be avoided whenever possible; and (5) volumes be kept small to avoid centrifuging, but when they are large, centrifugation should be for only 20 minutes at 3,000 r.p.m. *S. R. M. Bushby*

Desbordes, J., Fournier, E., Fournier, F. & Rosenberg, E. Contribution à l'ètude de la structure périphérique des Mycobactéries. [**Study of the Peripheral Structure of Mycobacteria**] *Ann. Inst. Pasteur.* 1959, Sept., v. 97, No. 3, 307–24, 4 figs. & 1 pl. [25 refs.]

In this study 2 virulent strains, an avirulent strain and 2 attenuated strains of tubercle bacilli were compared by (1) their X-ray diffraction patterns, before and after extraction with organic solvents and staining with Nile Blue; (2) their intensity of staining with Nile Blue and Turquoise pandurane, before and after progressive treatment with organic solvents, and with trypsin; and (3) their enzymatic activities.

The virulent strains produced many diffraction rings which decreased in number with progressive washing in acetone, ether, methanol and hot ethanol. The wavelength of these rings are given. In contrast, the number of rings produced by the avirulent strains was few, but it varied with the attenuated strains.

The virulent strains stained more intensely with Nile Blue than did the other strains, but whereas their staining became less with the progressive removal of lipids by the solvents, that of the BCG strain became more intense; with the Turquoise pandurane the staining effects were reversed. Treatment with trypsin also decreased the staining of the virulent strains with Nile Blue and the staining of the attenuated and avirulent strains with Turquoise pandurane.

After extraction with the organic solvents there was no definite reduction in catalase or urease activities but treatment with trypsin increased the dehydrogenase activities of the virulent strains.

These results are interpreted as showing that virulent strains have abundant peripheral lipoproteins with negative polaritis and whereas the attenuated strains have little surface lipoprotein they have deep ones which bind the metachromatic dyes; the avirulent strains have very few lipoproteins. *S. R. M. Bushby*

Von Bertrab, R. Untersuchungen über die Peroxydase- und die Katalaseaktivität frisch isolierter Tuberkelbakterien. [**Studies on the Peroxidase and Catalase Activity of Freshly Isolated Tubercle Bacilli**] *Schweiz. med. Woch.* 1959, Aug. 15, v. 89, No. 33, 868–70. [15 refs.]

There is abundant evidence in the literature that isoniazid-resistant strains of tubercle bacilli show diminished activity of the respiratory enzymes as well as diminished virulence for the guineapig.

The author set out to check these results with bacilli freshly isolated from patients under treatment. 133 strains from 101 patients were investigated. Isolations were made on the usual Löwenstein-Jensen medium containing 10 units penicillin/ml. and the determination of isoniazid resistance was carried out on Youmans fluid medium. The peroxidase test was carried out with a weak solution of catechol in acetate buffer *p*H 4·0 to which 0·3% peroxide was added. This mixture was poured on material taken from the surface of the culture on solid medium or on the washed supernatant from the fluid medium. Appearance of a brown to black coloration after 12–15 hours' contact was taken as a positive result.

The general outcome of these investigations was to show that the peroxidase reaction was more sensitive than the catalase reaction and better adapted to indicating the presence of mixed populations of resistant and sensitive bacteria. The more striking results were obtained with Youmans medium. Among 21 strains resisting concentrations of isoniazid of the order of 1–100 μgm. per ml. there were 20 peroxidase negative and 6 catalase negative, and among 78 strains of low resistance there were 8 negative peroxidase and one negative catalase. The interpretation which the author inclines to put on this finding is that the results with the 8 peroxidase negative strains among the strains of low isoniazid resistance probably indicate commencing development of resistance. *J. W. McLeod*

Hirsch, A., Cattaneo, C. & Maggini, P. Über den Aufbau der Mycobakterien. III. Der Nachweis von Stoffwechselvorgängen mittels elektronen-optischer Untersuchung von Ultradünnschnitten der Zellen verschiedener Mycobakterienspecies (Reduzierung von 2,3,5-Triphenyl-tetrazolium-chlorid). [**The Structure of Mycobacteria. III. Recognition of Metabolic Activities by means of the Investigations of Ultra Thin Sections of Cells of a Variety of Mycobacteria with the Electron Microscope. Reduction of 2,3,3-Triphenyl Tetrazolium**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 7/8, 514–31, 10 figs. on 5 pls. [26 refs.]

In earlier work already reviewed [this *Bulletin*, 1959, v. 34, 274] the saprophytic mycobacteria are distinguished from the virulent forms by their greater capacity to reduce triphenyltetrazolium salts to the stable coloured substance formazan.

This result is confirmed by the technique of embedding stained masses of bacteria in acrylic resins, cutting extremely thin sections, 100 Å, and examining these with the electron microscope for accumulations of the electron opaque material formazan. *J. W. McLeod*

HIRSCH, A. & CATTANEO, C. Die Mycobakterien: Chemischer Aufbau und Virulenz. IV. Die chromatographische Untersuchung der Aminosäuren im Zellhydrolysat der Mycobakterien verschiedener Species. [**Mycobacteria: Chemical composition and Virulence. IV. Chromatographic Studies of Amino Acids in Cell Hydrolysates of Mycobacteria of Different Species**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 7/8, 533–43, 4 figs. [30 refs.]

26 strains of mycobacteria classified by origin and by results of several virulence tests were hydrolysed by exposure to 105°C. for 14 hours in 6N HCl in closed tubes.

After removal of the HCl the residual amino acids were dissolved in iso propyl alcohol and the solution submitted to chromatographic analysis by the usual methods. Development of the paper strips was with ninhydrin and in all 20 different amino acids were recognized by well defined spots.

There were, in addition, 2 ninhydrin reacting substances of unknown character and 1 of these occurred constantly in virulent mycobacteria but not in saprophytic forms. Its exact nature was not determined.

[See also this *Bulletin*, 1958, v. 33, 1080.]

*J. W. McLeod*

ARIMA, J., YAMAMOTO, K., MOCHIZUKI, K. & TAKAHASHI, Y. Evaluation rapide de la virulence des bacilles tuberculeux par la méthode de culture de tissu. [**Rapid Evaluation of the Virulence of Tubercle Bacilli by the Method of Tissue Culture**] *C.R. Soc. Biol.* 1959, v. 153, No. 5, 883–7, 1 fig.

In this method tissue cultures are made of the spleens of guineapigs infected intravenously with 0·5 ml. of 14-day-old Dubos culture of the tubercle bacillus and after incubation counts are made of the bacilli present.

The present paper describes experiments in which comparison was made between the number of viable bacilli in the spleens of the guineapigs, immediately and at intervals up to 14 days after injection, with the number of bacilli in tissue cultures, after 0, 24 and 72 hours' incubation, of the spleens taken from the guineapigs immediately, 5 and 10 days after injection. The comparison was made with 9 strains of tubercle bacilli; these strains were H37Rv, H37Ra, BCG, 2 virulent human strains with 2 of their isoniazid-resistant variants, and 2 other virulent strains, 1 human and the other bovine. The number of viable bacilli present in the spleens was determined by culture of homogenates on egg medium.

The results show that not only was the increase in the number of bacilli in the spleens larger with the virulent strains than with the avirulent or attenuated strains, but also that only the virulent strains multiplied in the tissue cultures. The results also revealed no evidence of an immediate change in morphology after injection, that prevented their being demonstrated as typical acid-fast bacilli. *S. R. M. Bushby*

KATO, M., MIKI, K., MATSUNAGA, K. & YAMAMURA, Y. **Biochemical Analysis of the Virulence of Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1959, Oct., v. 80, No. 4, Pt. 1, 535–42, 1 fig. [26 refs.]

BURTIN, P. & KOURILSKY, R., with the technical assistance of J. URIEL & T. TERNYNCK. Recherches immunologiques sur les antigènes et haptènes solubles du bacille tuberculeux. I. Dénombrement et identification des constituants précipitant avec les immunsérums spécifiques. [**Immunochemical Studies on Soluble Antigens and Haptens of the Tubercle Bacilli. I. Isolation and Identification of the Components precipitating with Specific Immune Sera**] *Ann. Inst. Pasteur.* 1959, Aug., v. 97, No. 2, 148–70, 1 diagram & 7 figs. [34 refs.]

This is an extensive investigation of the precipitating antigens present in various extracts of culture filtrates and autolysates of the bacilli of H37Rv and a bovine strain 1099. The antigens were detectable by the immuno-electrophoretic analytical method of GRABAR and WILLIAMS (*Biochim. et Biophys. Acta.*, 1955, v. 17, 67) by using sera from rabbits injected with heat- and phenol-killed tubercle bacilli suspended in liquid paraffin.

Of the precipitating antigens identified in the products of H37Rv, 2 were definitely polysaccharides and 1 of these was identical with SEIBERT'S polysaccharide I [this *Bulletin*, 1949, v. 24, 524]. The other was derived from a lipopolysaccharide and the authors suggest that this should be called polysaccharide III; it is apparently identical with that of PMKO of CHOUCROUN [*ibid.*, 1948, v. 23, 447]. A third antigen was also probably a polysaccharide and this may be Seibert's polysaccharide II. 3 or perhaps 4 protein antigens were detected; they were all heat labile and precipitated by trichloracetic acid and slowly hydrolysed by trypsin; 1 of these was identified as Seibert's C protein [*ibid.*, 1955, v. 30, 1017].

The culture filtrates of the bovine strain contained less polysaccharide III than did those of the human strain, and 1 of the proteins was not detected. Old Tuberculin contained only the polysaccharides I and II.

As the preparations used in these studies were incapable of producing antibodies, none of the antigens can be regarded as full-antigens and are presumably degradation products of more complex molecules.

*S. R. M. Bushby*

BURTIN, P., with the technical assistance of J. URIEL & T. TERNYNCK. Recherches immunochimiques sur les antigènes solubles du bacille tuberculeux. II. Étude immunochimique de deux polysaccharides présents dans les filtrats de culture du bacille tuberculeux. [**Immunochemical Studies on Soluble Antigens of Tubercle Bacilli. II. Immunochemical Studies of Two Polysaccharides present in Culture Filtrates of Tubercle Bacilli**] *Ann. Inst. Pasteur.* 1959, Sept., v. 97, No. 3, 325–39, 2 figs., 1 diagram & 1 pl. [27 refs.]

The soluble antigens used were the Polysaccharides I and III. The samples of polysaccharide I were from 4

samples of tuberculin, obtained by precipitation with 9% ethanol and extraction with phenol, and a sample of haemosensitin of SORKIN and BOYDEN [this *Bulletin*, 1956, v. 31, 205]. The polysaccharide III was obtained by hydrolysis of the fraction of lipopolysaccharide of PMKO of CHOUCROUN [this *Bulletin*, 1948, v. 23, 447] and 3 samples of the polysaccharide of ASSELINEAU *et al.* (*Bull. Soc. Chimie Biol.*, 1958, v. 40, 1953). The antigens were examined by the agar-gel diffusion technique and by electrophoresis using immune serum and globulins from rabbits injected with tubercle bacilli. Quantitative estimations were made by mixing the antigens together, collecting the precipitate and estimating it by the biuret method.

Both the diffusion and electrophoretic methods showed that the various samples of the 2 polysaccharides were identical, irrespective of whether they were from human or bovine strains. The 2 polysaccharides were apparently immunologically distinct although they were related, and antisera reacted with only one or both of the antigens. Cross-neutralization tests showed that with some antisera 1 of the polysaccharides completely or partially neutralized the antibodies of the other but with the other sera there was no neutralization; the relative amounts of precipitate with the 2 polysaccharides also varied with different samples of antisera. The addition of galactose, arabinose and mannose to 1 of the samples of antisera caused a slight reduction of the precipitate, especially when the latter 2 sugars were added together but no neutralization occurred with the other sera.

Possible explanations of these results are discussed.

*S. R. M. Bushby*

MACKEPRANG, B. & JESPERSEN, A. **Use of Ultrasonic-Treated Suspensions of Tubercle Bacilli for Determination of Infection Doses in Animal Experiments.** *Acta Path. et Microb. Scandinavica.* 1959, v. 46, No. 1, 73–84. [12 refs.]

In this experiment the E6884 strain of bovine tubercle bacilli grown in Dubos medium was exposed to ultrasonic vibration at an intensity of 0·56 watt/cm.$^2$ for 10 and 60 minutes. Stained smears and viable counts were made of the suspensions before and after the treatment, and groups of red mice were injected intravenously with 10-fold dilutions of them. All the mice dying during the experiment and those killed on the 232nd day, when the experiment was terminated, were examined for gross tuberculous lesions.

The stained films showed that whereas 46% of the bacilli were present as single cells and 34% in clumps of 3–4 bacilli before the ultrasonic treatment, 86% and 94% were present as single bacilli, the remainder being in clumps of not more than 4 bacilli, after 10 and 60 minutes' treatment, respectively. These decreases in aggregate size produced an approximately 10-fold increase in the number of viable units but there were decreases of 7% and 34% respectively, in germination of the 10- and 60-minute-treated suspensions.

The mouse experiment showed: (1) that 1 bacillus was sufficient to cause fatal tuberculosis in this strain of mice; (2) that exposure to ultrasonic vibration causes no loss of virulence—in fact, mice injected with the treated suspensions died more quickly than those injected with the untreated suspensions; and (3) that either Löwenstein-Jensen medium, Dubos oleic-acid-albumin-agar or the red mouse offer equally good conditions for growth of the bacillus used in these experiments.

*S. R. M. Bushby*

SÁNDOR, I. **On the Role of the Reactivity of the Infected Organism in the Development of Tuberculosis. (Studies on Embryonic Tissues.)** *Acta Morphologica.* Budapest. 1959, v. 9, No. 1, 89–103, 12 figs. [38 refs.]

The aim of this investigation was to study the morphogenesis of the disease in terms of the reactivity of the tissues of the embryonic host. The chick embryo was chosen not only for convenience but also because the effects observed in it are not confused by the presence of maternal reactions. The embryonic eggs were infected with tubercle bacilli by various routes from the 4th to the 13th day of incubation.

Histological examination showed a metaplasmic response by the epithelium of the chorio-allantoic membrane to infection at that site whereas the epithelium of the embryo showed little or no response to a similar infection. There was also infiltration of mesenchymal tissue, giant cell formation and necrosis in the membrane but little or none of these changes occurred in the embryo. [The morphology of these giant cells and the type of necrosis were considered to be unusual, but the differences are not specifically described.] No specific reactions were observed in the organs of the embryo after an intravenous injection given on the 12th–13th day, but as specific tuberculous changes usually take 9–10 days to develop and the eggs had hatched by this time, the period of observation was probably too short to exclude the possibility of specific changes developing. Specific focal changes were, however, observed in the chick 4–23 days after hatching, suggesting a sudden change in systemic reactivity after hatching.

Haematological examination showed neutrophilia, eosinopenia and lymphopenia on the 18th–20th day.

In general, it would therefore appear that the reactivity of the embryo differs greatly from that of the chorio-allantoic membrane to the presence of the tubercle bacillus.

*S. R. M. Bushby*

EIDUS, L., DIENA, B. B. & GREENBERG, L. **The Tuberculostatic Activity of Intermediate Compounds of Chloramphenicol.** *Antibiotics & Chemotherapy.* New York. 1959, Aug., v. 9, No. 8, 491–6.

These authors tested the action on *Mycobacterium tuberculosis* H37Rv of 11 intermediate compounds in the synthesis of chloramphenicol. 1 had the same activity as chloramphenicol itself, inhibiting growth at 10 μgm./ml. and 1, *p*-nitro-α-acetylamino-β-hydroxypropiophenone, was inhibitory at 2 μgm./ml. 4 other compounds closely related to this had lesser activity or none. This activity was equal against human and bovine strains, but avian and atypical strains and 3 other species of *Mycobacterium* were much more resistant, being inhibited only by 80 or 160 μgm./ml.

*L. P. Garrod*

GUPTA, K. C., PANISSET, M., BENOIT, J. C. & FRAPPIER, A. Un caractère différentiel des sous-souches du B.C.G. [**A Differentiation Character of the BCG Substrains**] *Ann. Inst. Pasteur.* 1959, Sept., v. 97, No. 3, 340–45, 3 figs.

By adding an aqueous solution of the 2,3,5-triphenyl tetrazolium chloride to 21-day cultures of BCG, growing on solid Dubos medium, sub-strains of this bacillus have differences in their ability to form formazan, shown by variations in colour of their colonies. The variations were not related to the type of colony, *i.e.* whether spreading or rough, or to the amount of formazan formed by suspensions of the bacilli.

*S. R. M. Bushby*

PANISSET, M. & BENOIT, J. C. Survie et multiplication du BCG et du bacille tuberculeux chez la souris en fonction du temps. I.—Étude d'une méthode de mesure. [**Survival and Multiplication of BCG and Tubercle Bacillus in Mice in Relation to Time Factor**] *Ann. Inst. Pasteur.* 1959, Oct., v. 97, No. 4, 437–52, 4 figs. [18 refs.]

Details are given of the methods of growing BCG and H37Rv, of caring for and feeding the mice, and of making the viable counts on the spleens, lungs and livers of the infected mice. Vaccination with 15,000 viable units of BCG was made by injection into the jugular vein, under nembutal anaesthesia.

The results of the viable counts on the vaccinated animals showed that the number of BCG in the spleen increased during the first 3 weeks by approximately 100-fold and then decreased rapidly, so that by the 7th week the number present was no more than during the first week. The number of bacilli in the liver also rose, and although after 1 week it was 6 times more than in the spleen, the actual increase was only 4-fold; the number in the lungs after 1 week was only about one-third of that present in the spleen but it represented an increase of 60-fold.

Counts made of the total number of tubercle bacilli present in the tissues 3, 4, 7 and 11 weeks after vaccination with BCG and 2 weeks after challenge with 5,000 viable units of H37Rv, showed that the maximum number of bacilli was also present at the 3rd week and fell markedly by the 7th week.

A third experiment, designed to show the effects of the age of the mouse on the number of bacilli present in the tissues 15 days after injection with H37Rv, showed that although the numbers of bacilli in the tissues of 1- and of 2-week-old mice were not very different, they were certainly less in 9-week-old mice; the numbers in the spleen and lungs were only about one-third, and in the liver about one-tenth, of those in the younger mice, thus showing that quite apart from effects of immunization, age alone can affect the multiplication of the bacilli in the mouse.

These results are discussed and the authors conclude that for following the number of tubercle bacilli in the mouse, counts of those present in the spleen are adequate.

*S. R. M. Bushby*

GRUMBACH, Françoise. La souris, animal de diagnostic pour différencier les souches de bacilles tuberculeux avirulentes ou de virulence atténuée pour le cobaye (souches BCG, souches dites "atypiques", souches isoniazido-résistantes). [**Inoculation into Mice as a means of Diagnostic Differentiation between Tubercle Bacilli Avirulent or Attenuated for Guineapigs (BCG, Atypical, Isoniazid-Resistant Strains)**] *Ann. Inst. Pasteur.* 1959, Oct., v. 97, No. 4, 453–65, 2 text figs. & 6 figs. on 3 pls. [15 refs.]

The bacilli were grown in Dubos medium for 6–8 days and 0·5 to 1·0 mgm. (wet weight) of the culture was inoculated intravenously into groups of 12 30-day-old mice of a strain that was regularly killed in 20–25 days by 0·05 mgm. H37Rv. The lungs, kidneys and spleens of the animals were examined histologically and for viable bacilli.

30 different strains of BCG were examined; 5 of them produced no lesions and the most constant lesion produced by the others was in the kidneys. The animals were killed from the 8th to the 18th month after infection; the kidneys were enlarged 5–10 times and contained caseous abscesses in which were many acid-fast bacilli. Re-inoculation of the bacilli into fresh mice produced only the same type of lesion. Although only minimal pulmonary lesions were produced by most of the strains, 3 produced definite lesions.

19 strains of "atypical" bacilli were examined. 7 were photochromogens and they caused the death of the mice in 18–80 days, producing pulmonary and renal lesions similar to those produced by H37Rv. 6 were scotochromogens and only 1 of these produced lesions and it was recoverable from the mice 10–21 months later; it caused scarring in the kidneys. 2 of the strains were non-photochromogens; 1 killed the mice in 8–16 months producing few or no lesions in the lungs but severe caseation in the kidneys; the other strain killed the mice in 9–14 months, and although there were only minimal pulmonary lesions and no macroscopic lesions in the kidney, there were numerous bacilli in these organs and in the spleen.

4 strains were *Mycobacterium balnei* and these produced lesions only in the tails and paws, and they developed in 20–30 days.

In this study, no isoniazid-resistant strains of tubercle bacilli were examined but the author quotes his previous work in which these strains were shown to kill the mice after varying intervals and to produce persistent pulmonary lesions but no renal lesions. *S. R. M. Bushby*

JESPERSEN, A. & MACKEPRANG, B. **Immunity and Tuberculin Sensitivity in Guinea Pigs vaccinated with a Known Number of Viable BCG in Coarse Suspensions and Finely Dispersed Suspensions dispersed by means of Ultrasonics.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, No. 3, 245–60, 1 fig. [14 refs.]

The BCG was grown in Dubos medium and after being well shaken it was shown to contain $30 \times 10^6$ viable units/ml. and 53% of the bacilli were shown to be aggregates of more than 5 bacilli. After exposure to ultrasonic vibrations for 10 minutes at 0·56 watt/cm$^2$, the number of viable units was increased almost 10-fold

and 87% of the aggregates were then single bacilli with none containing more than 5 bacilli. These suspensions were diluted $10^{-4}$, $10^{-5}$, and $10^{-6}$ and 2 × 0·1 ml. quantities were inoculated intracutaneously into groups of 20 guineapigs. The animals were tested 85–88 days later with 5 and 250 T.U. of tuberculin and on the 91st day they were challenged intravenously with $10^{-5}$ mgm. of virulent bovine bacilli.

The results show that with small inocula of BCG, the size of the bacillary aggregate affects the development of hypersensitivity; 50% of the animals became tuberculin-positive after vaccination with 150 viable units of BCG in finely dispersed suspension, whereas 450 bacilli in coarse suspension were needed to produce the same result. With large inocula the degree of dispersal had no effect on the development of hypersensitivity.

Vaccination had no effect on immunity unless the animals became tuberculin-positive, and then neither the size of the vaccination dose nor its state of dispersion affected the degree of immunity.

*S. R. M. Bushby*

MACKEPRANG, B. **Vaccination of Guinea Pigs with Coarse and Finely Dispersed BCG Suspensions dispersed by means of Ultrasonics.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, No. 3, 261–72. [12 refs.]

The BCG suspensions used in these experiments were prepared by the method described in the previous paper [see above] and the dispersal effects of the ultrasonic treatment were similar, the number of viable units being increased 6·5 times and the germination percentage decreased to 85. Groups of 12 guineapigs were vaccinated at 2 sites with 0·1 ml. of these suspensions, undiluted and diluted 1:10. The animals were tested with 5 TU of tuberculin 60 days after vaccination, and 2 days later they were challenged with $10^{-5}$ mgm. of virulent bovine tubercle bacilli, injected intravenously.

The only difference observed between the groups receiving the fully dispersed vaccine and those receiving the coarsely dispersed one was that formation of abscesses and pus at the vaccination site occurred less frequently with the finely dispersed suspension; the swelling of the draining lymph gland, the development of hypersensitivity and the degree of immunity were apparently not related to the dispersed state of the vaccine.

Also, no relationship was demonstrated between immunity, on the one hand, and the development of primary reactions, the duration of the glandular swelling and the size of the tuberculin reaction on the other hand.

*S. R. M. Bushby*

ENGBAEK, H. C., MAGNUSSON, M. & NIELSEN, J. A. **A Further Case of Lung Disease caused by an Atypical Acid-Fast Organism.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, No. 3, 227–44, 3 figs. [19 refs.]

This report is of a 56-year-old patient who had been X-rayed with negative results in 1952 and 1954 but was tuberculin-positive. In 1955 a further X-ray, taken after a year's increasingly severe dry cough, fatigue and dyspnoea, showed slight infiltration in the first right intercostal space; examination of gastric lavage was negative. X-ray examination showed no change until July, 1956, when progression was observed and the patient entered hospital. He was apyrexial and tomographical examination revealed a 15 mm. cavity in the right apex. Acid-fast bacilli were grown from gastric lavage specimens and treatment with 1 gm. streptomycin every third day, 100 mgm. isoniazid, and 4 gm. PAS 3 times daily was given. The patient gained weight, the red cell sedimentation rate decreased and the X-ray showed some clearing. From February, 1957, treatment was continued at home, but X-ray examination in May, 1957, revealed progression of the disease with enlargement of the cavity. Cycloserine was added to the chemotherapy and resection of the apical segment was made. Tuberculin tests made in November, 1957, showed that he reacted more strongly to avian tuberculin and tuberculin made from the autogenous strain, than did tuberculous patients. In January, 1957, his general condition was good, X-ray normal and gastric-lavage negative.

The histological examination of the resected specimen showed lung tissue with extensive chronic fibrocaseous tuberculous changes.

The acid-fast bacillus took 4 weeks to grow on Löwenstein-Jensen medium; the growth was yellowish and the colour did not increase on exposure to light. Before the commencement of treatment, the bacillus was sensitive to cycloserine, but more resistant than a standard strain of tubercle bacilli to streptomycin (x4), isoniazid (x64) and viomycin (x16), and it was highly resistant to PAS. It was negative for niacin and moderately positive for catalase. During treatment it became highly resistant to streptomycin. In animals, it caused chronic infection in rabbits and mice, and only local and regional infection in guineapigs. Skin reactions in guineapigs, vaccinated with various strains of mycobacteria, to the PPD from this strain suggested that it was related to the Battey type of atypical acid-fast bacilli [this *Bulletin*, 1957, v. 32, 659], rather than to human, bovine or avian tubercle bacilli or the photochromogens.

*S. R. M. Bushby*

VIALLIER, J. & CAYRÉ, R. M. Sur les caractères antigéniques de mycobactéries non pathogènes. **[The Antigenic Characteristics of Non-Pathogenic Mycobacteria]** *C.R. Soc. Biol.* 1959, v. 153, No. 6, 1031–3.

The sera of 2 guineapigs and 1 hen inoculated with a "yellow atypical" mycobacterium isolated from a patient who had died of non-tuberculous pulmonary disease, produced agglutinin titres of 1:80 for the autogenous strain but only 1:20 or less for human tubercle bacilli; rats and mice inoculated with the organism did not produce agglutinins for either of the mycobacteria. Guineapigs inoculated with tubercle bacilli, and guineapigs and hens inoculated with saprophytic mycobacteria produced agglutinins to similar titre for both the "atypical" mycobacterium and the tubercle bacillus.

The sera of 12 of 13 tuberculous patients agglutinated the "atypical" mycobacterium and tubercle bacilli to similar titres; the serum of the 13th patient

agglutinated neither organism. The sera of 4 tuberculin-negative persons did not agglutinate the tubercle bacillus, but 1 of the sera agglutinated the "atypical" bacillus to a titre of 1:80. 5 of the sera of 7 other tuberculous patients, agglutinated both the "atypical" bacillus and the tubercle bacillus but none agglutinated the saprophytic bacillus.

The "atypical" mycobacterium was inoculated subcutaneously into 8 guineapigs, and 21 days later the animals were injected intradermally with tubercle bacilli; neither a Koch phenomenon nor an allergic tuberculin reaction occurred at the site of the superinfection.

*S. R. M. Bushby*

LUGOSI, L. La capacité des mycobactéries saprophytes de tolérer $H_2O_2$ (indiquée par le changement du potentiel d'oxydo-réduction) et ses rapports avec leur sensibilité à l'INH et leur activité catalasique. [**The Capacity of the Saprophytic Bacteria to Tolerate $H_2O_2$ (shown by the Change in Oxidation-reduction Potential), in Relation to Their Isoniazid Sensitivity and Catalase Activity**] *Ann. Inst. Pasteur.* 1959, Oct., v. 97, No. 4, 597–606, 4 figs. [17 refs.]

This examination was made on 3 strains, and a variant of different isoniazid-sensitivity derived from each. The organisms were *Mycobacterium frieburgensis* and *Myco. phlei*, both of which were sensitive to 1 μgm. isoniazid and their variants resistant to 80 μgm./ml., and *Myco. pellegrino* which was resistant to 2,500 μgm./ml. and its variant which was resistant to only 80 μgm./ml. The catalase activity was measured chemically by determining the residual peroxide present at intervals after adding $H_2O_2$ to a suspension of the bacillus in a buffer solution; sensitivity to the peroxide was obtained by measuring the effects of adding 1,000 μgm. of $H_2O_2$ per ml. at various stages of growth on the normal fall in the oxidation-reduction potential of the culture.

The results show that the catalase activity of each of the variants was greater than that of the parent strain and that whereas the respective metabolism of the parent strain of *Myco. phlei* and its variant was little affected by the peroxide, that of *Myco. frieburgensis*, *Myco. pellegrino* and their variants was markedly reduced when the peroxide was added during the lag phase of growth but not when added during the logarithmic phase; the inhibiting effect was greatest with the variant of *Myco. frieburgensis* and with the parent strain of *Myco. pellegrino*.

Differences in the sensitivity of these saprophytes to hydrogen peroxide is thus not directly related to catalase activity or to sensitivity to isoniazid.

[See also this *Bulletin*, 1956, v. 31, 1158; 1957, v. 32, 802, *bis*.] *S. R. M. Bushby*

MCFADZEAN, J. A. & VALENTINE, R. C. **The Value of Acridine Orange and of Electron Microscopy in determining the Viability of** *Mycobacterium leprae murium*. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, Sept., v. 53, No. 5, 414–22, 4 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 141.]

BRANHAM, Sara E., HIATT, C. W., COOPER, A. D. & RIGGS D. B. **Antigens associated with the Toxin of the *gravis* Type of** *Corynebacterium diphtheriae*. *J. Immunology.* 1959, May, v. 82, No. 5, 397–408, 7 figs. [34 refs.]

The emphasis in the literature on the prominence of oedema of the tonsils and neck in diphtheria due to *gravis* strains and the fact that this variant of *C. diphtheriae* has recently played a considerable part in the malady in the U.S.A., have led the authors to look for factors other than the classical toxin common to all diphtheria bacilli. 2 *gravis* strains G1 and G2 were selected for comparison with a standard PW 8 strain.

Toxin was produced on 14-day incubation in a modified Mueller medium and it was found that the PW 8 toxin was more potent than the others and contained a lower proportion of total solids and of nitrogen.

It was noted, however, that the guineapigs killed in the process of establishing the MLD and L+ doses of these toxins showed oedema of peritoneum and pleurae to a greater extent after injection of G1 and G2 than after PW 8. This phenomenon was most marked with G2.

Observations on immune electrophoresis and ultracentrifugation indicated that this oedema-producing activity was associated with a component of high molecular weight travelling very slowly in the electrophoretic field which was not recognized in the PW 8 toxin.

No evidence of the spreading factor "B" described by O'MEARA [this *Bulletin*, 1947, v. 22, 349] was obtained, however. The need for further study of toxic factors other than the classical toxin produced by strains of *C. diphtheriae* is emphasized.

*J. W. McLeod*

RELYVELD, E. H. & RAYNAUD, M., with the technical collaboration of O. BEPOLDIN. Étude quantitative de la réaction entre la toxine diphtérique et divers sérums antidiphtériques de faible pouvoir neutralisant. [**Quantitative Studies of the Reaction between Diphtheria Toxin and Different Anti-Diphtheria Sera of Low Neutralizing Capacity**] *Ann. Inst. Pasteur.* 1959, May, v. 96, No. 5, 537–47, 5 figs. [25 refs.]

These were sera obtained from horses with low basic immunity and even the fraction rich in gamma globulin obtained by precipitation with $(NH_4)_2SO_4$ at 33% level of saturation gave a ratio of L+/Lf considerably below 1.

Curves are recorded which were calculated on the protein N content of the precipitate thrown down when increasing amounts of toxin were added to a fixed quantity of antiserum. Maximum precipitation was obtained at a point beyond that of optimum precipitation from which the Lf is determined and the L+ point was obtained with even less toxin.

Determinations were made both *in vivo* and *in vitro* of the toxic action of both the precipitates and the supernatants from which these had been separated. The presence of active toxin was demonstrated by Jerne's test, intradermal injection in a white rabbit, in the precipitates from the mixtures at L+ level and

from those containing higher proportions of toxin. This is to say that toxic effects were obtained by precipitates formed in presence of excess of antibody which could be demonstrated in the supernatant.

Toxic activity was not observed in the supernatants, however, until the summit of the curve, maximum precipitation of the toxin, had been passed. The authors consider that the observation of toxic action with these fractions containing excess of antibody is incompatible with POPE's hypothesis [this *Bulletin*, 1952, v. 27, 478; 1953, v. 28, 485] of a group of protein antigens closely related to the specific toxin and associated with it but distinct from it which give rise to flocculation with antisera and high Lf values independent of specific toxin neutralization.

As an alternative hypothesis they suggest a single toxin molecule carrying many antigenic facets most, or all but 1, of which lack toxic action. They argue that the toxin would not be carried down in an aggregate of non-specific antibody-antigen precipitate.

*J. W. McLeod*

CIUCĂ, M., POPOVICI, Marcella, SARAGEA, Alice, MAXIMESCO, Paula, & NOVAC, Stela. Potentiel de "variation" et capacité d'adaptation entrecroisée des bactériophages:—antistaphylococciques et antidiphtériques—sur des souches homologues ou hétérologues, soumises à la "lysogénéisation". **[Potential of "Variation" and Capacity of Crossed Adaptation of Staphylococcus and Diphtheria Bacteriophages to Homologous and Heterologous Strains Subjected to "Lysogenization"]** *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 595–612, 7 figs.

The observations of HEWITT and others on the possibility of adapting the bacteriophage appropriate to one bacterial species to an entirely distinct one are confirmed.

By taking 7 strains of *Corynebacterium diphtheriae* sensitive to bacteriophage lysis and trying out a variety of staphylococcal bacteriophages on them, zones of opaque lysis, OL, were obtained on 2, and when subcultures from lysed areas and the surrounding fringe of culture were made in Pope-Linggood broth without sugar the activity of the bacteriophage could be raised so that it acted on a variety of diphtheria strains and sometimes even at a dilution of $10^3$.

The bacteriophage so adapted to the *C. diphtheriae* had lost its activity for the staphylococcus, and this could not be restored by subsequent passage on strains of staphylococcus which had served as indicator strains for the original staphylococcal bacteriophage.

The reverse change was successfully carried out, the *C. diphtheriae* bacteriophage 67 was adapted to the staphylococcal strain 73. The bacteriophage so obtained "F St. 7" was actually capable of acting on strain 73 at dilution of $10^5$ and had very trifling residual activity against *C. diphtheriae* strains. It differed, however, from the staphylococcal phage strains adapted to *C. diphtheriae* in the respect that its power of lysing diphtheria strains could be readily restored by appropriate passage.

*J. W. McLeod*

CIUCĂ, M., SARAGEA, Alice, MAXIMESCO, Paula, MEITERT, Eugenia, IERIMIA, T. & CALALB, G. Lysogénie et pathogénité dans la biologie du corynebacterium diphtheriae. Rôle inducteur du bactériophage diphtérique dans le procès de variation du bacille diphtérique de l'état d'avirulence vers la virulence-toxinogénèse. **[Lysogenicity and Pathogenicity in the Biology of *C. diphtheriae*. The Inducing Role played by the Diphtheria Bacteriophage in the Process of "Variation" of the Diphtheria Bacillus from Avirulence to Virulence-Toxigenicity.** *Arch. Roumaines Path. Expér. Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 613–26. [23 refs.]

Many variants were prepared from 4 diphtheria strains, all non-toxigenic and of *mitis* type, by submitting them to the action of a wide range of bacteriophages derived from diphtheria strains and 1 staphylococcal bacteriophage adapted to *Corynebacterium diphtheriae*.

An extensive study of the derived strains showed wide variations in respect of fermentation, sensitivity to lysis, lysogenicity, toxinogenesis and haemolysis.

3 of the strains, 1 from a carrier and 2 obtained from Warsaw, gave no variants which departed from the *mitis* colony type and only 1 variant is recorded as fermenting starch. The fourth strain, obtained from a case of diphtheria in a village in Rumania, showed much wider variation in its derived strain including some *gravis* and *intermedius* types of colony usually associated with capacity to ferment starch.

The largest proportion of conversions of atoxigenic to toxigenic strains was obtained with the adapted bacteriophage of staphylococcal origin.

*J. W. McLeod*

MATSUI, T. & KUWAJIMA, Y. **Formation of the Toxoid of Histamine Sensitizing Factor in** *Bordetella pertussis*. [Correspondence.] *Nature*. 1959, July 18, v. 184, Suppl. No. 4, 199–200.

The authors believe that the histamine sensitizing factor of *Bordetella* [*Haemophilus*] *pertussis* organisms is a toxin different from the accepted *pertussis* toxin and they claim to have prepared toxoid from this toxin by treatment with formalin.

Formalin (0·5%) was added to the supernatant fluid from a culture of *Bordetella pertussis* 18–323. After various intervals of incubation at 37°C., samples were removed and tested for loss of the histamine sensitizing factor. It was found that heating the supernatant fluid at 56°C. for 30 minutes did not destroy the histamine sensitizing factor, whereas heating at 37°C. with formalin partially destroyed it in 4 days and completely destroyed it in 7 days. Mice surviving the histamine sensitivity test were inoculated 14 days later with either pertussis vaccine or supernatant fluid and subsequently challenged with histamine to determine their immunity to the sensitizing factor. The mice inoculated with supernatant fluid, treated with formalin for 7 days, were found to be immune and although prolonged periods of treatment with formalin had destroyed the histamine sensitizing factor the mice inoculated with these samples were not immune.

*F. T. Perkins*

PEKÁREK, J. & ŘEZÁBEK, K., with the technical assistance of H. HAISOVÁ, G. PEKÁRKOVÁ & V. STEJSKAL. **The Investigation of Different Components of Pertussis Vaccine obtained by Centrifugation.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 1, 67–78, 1 diagram. [11 refs.]

4 components of a fluid pertussis vaccine: (A) the original vaccine, (B) the supernatant fluid, (C) the sediment remaining after centrifugation, and (D) the washed sediment, were compared for their ability to protect mice against intracerebral challenge with pertussis organisms.

Although the authors found that some protective antigen was present in the supernatant fluid, the washed organisms were still protective, and they believe that centrifugation and washing of the deposit can be recommended in the production of effective pertussis vaccines. *F. T. Perkins*

PEKÁREK, J. & ŘEZÁBEK, K., with the technical assistance of H. WIESNEROVÁ & V. NOVÁ. **An Endocrinological Test for Innocuity of the Pertussis Vaccine.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 1, 79–84. [11 refs.]

The authors attempted to design a test to measure the degree of adverse reactions caused by pertussis vaccines which they have called the "reactogenicity".

In their experiments toxic vaccines and vaccines detoxified by prolonged storage were used and the stress effects of the different components, obtained by centrifugation, were tested.

The reactogenicity was measured by the decrease of ascorbic acid in the adrenal glands in rats and it was found that the stress-producing component was lost by long storage of vaccine or by centrifugation of organisms from the supernatant fluid. The results were in agreement with those of tests based on the study of weight changes in guineapigs and mice although more rapid and definite results were obtained by the tests on decrease of ascorbic acid in the adrenal glands. *F. T. Perkins*

KIND, L. S. **Sensitivity of *pertussis* Inoculated Mice to Endotoxin.** *J. Immunology.* 1959, Jan., v. 82, No. 1, 32–7, 1 fig. [15 refs.]

The author deals with various aspects of endotoxin sensitivity in mice inoculated with *Haemophilus pertussis* vaccine, its duration, its possible relation to bacterial infection and its inhibition by previous sublethal injections.

It was found that the rise and fall of sensitivity to endotoxin in the vaccinated mouse parallels closely the development of histamine and serotonin susceptibility in such animals. 13 days after vaccination, mice possessed an enhanced susceptibility to the lethal effects of *Escherichia coli* endotoxin as well as to living *E. coli* organisms. Preliminary injections of sublethal amounts of *E. coli* or *Serratia marcescens* [*Chromobacterium prodigiosum*] endotoxins, however, restored their resistance to subsequent challenge with lethal doses of *E. coli* endotoxin. On the other hand the preliminary injections of *E. coli* endotoxin did not prevent mice inoculated with pertussis vaccine from developing an increased susceptibility to histamine or anaphylactic shock. *E. coli* endotoxin was found to potentiate the development of anaphylactic sensitivity in these mice although it did increase the resistance of vaccinated mice to subsequent injections of the vaccine.

[See also this *Bulletin*, 1953, v. 28, 752.]

*F. T. Perkins*

BOYER, F. & CHEDID, L. Production d'une source abondante d'anticorps dans le liquide d'ascite obtenu par greffe du carcinome d'Ehrlich à la souris vaccinée avec *Hemophilus pertussis*. [**Production of High Antibody Levels in Ascitic Fluid obtained by means of Transplantation of Ehrlich Carcinoma into Mice immunized against** *Haemophilus pertussis*] *Ann. Inst. Pasteur.* 1959, May, v. 96, No. 5, 643–7, 1 fig.

An inoculation of Ehrlich carcinoma into mice previously immunized with *Haemophilus pertussis* organisms resulted in the production of ascitic fluid with high agglutinin levels to *H. pertussis*. The carcinogenic property of the ascitic fluid could be destroyed with 0·4% formalin without decreasing the pertussis agglutinin titre. An abundant source of antibody is thus easily induced in mice.

[It is difficult to understand why one should be exposed to the hazard of handling a carcinogenic fluid when conventional methods are capable of producing large volumes of serum with high antibody levels.]

*F. T. Perkins*

HUET, M. L'uréase et la lysine-décarboxylase de *Haemophilus influenzae* et des espèces apparentées. [**Urease and Lysine-decarboxylase in** *Haemophilus influenzae* **and Related Species**] *Arch. Inst. Pasteur de Tunis.* 1959, Mar., v. 36, No. 1, 29–35.

Strains of *Haemophilus influenzae* have been shown to have high urease activity which greatly facilitates identification of the organism from conjunctival swabs and 15% of the strains had a lysine-decarboxylase activity. The author confirms that 3 strains of *Haemophilus aegyptius* examined also had a high urease activity.

So far it is not possible to draw any conclusions from the urease and the lysine-decarboxylase activities of strains of *Haemophilus para-influenzae*.

*F. T. Perkins*

OLITZKI, A. L. & SULITZEANU, Ada. **Antigenic Structures of *Haemophilus aegyptius* and *Haemophilus influenzae* demonstrated by the Gel Precipitation Technique.** *J. Bacteriology.* 1959, Mar., v. 77, No. 3, 264–9, 1 fig.

The soluble antigens present in sonic extracts of *Haemophilus aegyptius* strains, isolated from pathological conditions of the conjunctiva in Israel and the United States, with suitable hyper-immune sera, gave almost identical serological reactions with almost the same 10 precipitation lines in agar gel.

On the other hand, *H. influenzae* antigens in contact with *H. aegyptius* immune sera, never showed more

than 4 precipitation lines identical with those produced by *H. aegyptius* extracts.

All *H. aegyptius* extracts in the presence of *H. influenzae* immune sera produced 1 to 3 additional lines which were not produced by *H. influenzae* antigens themselves. This phenomenon indicated that certain additional antigens, although present in *H. influenzae* extracts in sufficient quantities to give rise to antibody production after a long immunization period, were nevertheless not sufficiently concentrated to produce visible precipitation lines. Their concentration in *H. aegytius* extracts was sufficient to produce visible precipitation lines.

Although sonic extracts of *H. aegyptius* and *H. influenzae* contained many common antigens, the two species could be differentiated by species-specific antigens which gave rise to specific precipitation lines in reactions with homologous sera. *F. T. Perkins*

PATON, A. M. **Enhancement of Pigment Production by** *Pseudomonas*. [Correspondence.] *Nature*. 1959, Oct. 17, v. 184, Suppl. No. 16, 1254, 1 fig.

SMITH, H. G. **On the Nature of the Selective Action of Selenite Broth.** *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 61–71, 2 figs. [15 refs.]

Sodium selenite, in concentrations of 1%, is toxic for bacteria in general within the family Enterobacteriaceae. In concentrations of 0·5%, however, selenite broth is a selective medium which is widely used for the routine isolation of salmonella organisms. This medium was introduced by LEIFSON (*Amer. J. Hyg.*, 1936, v. 24, 423), but it was shown by H. W. SMITH in 1952 [see this *Bulletin*, 1952, v. 27, 786] that it was not a satisfactory enrichment or selective medium for *Salmonella cholerae suis*. This important observation is fully confirmed in this paper for whereas few *Salm. cholerae suis* survived in media where the concentration of sodium selenite was 0·1%, *Salm. typhi* and *Salm. typhimurium* flourished. When the selenite broth was treated with charcoal for the adsorption of the peptides the depleted medium failed to support the growth of *Salm. typhi* and *Salm. cholerae suis* and only permitted slight growth of *Salm. typhimurium*, but the peptone medium without selenite, treated with charcoal, allowed good growths of *Salm. typhimurium* although the other two failed to grow. This fact suggests that the peptides can protect the organism against the toxic effects of the selenite and that these substances confer a degree of selectivity on the selenite medium. The intensity of the reduction of selenite to selenium was associated with the peak logarithmic phase of growth of the organism and this was roughly parallel with $H_2S$ production. Although the intensity of reduction is related to the profuseness of growth many organisms do not survive the reducing conditions. The utilization of different sulphur sources varied; in defined "sulphur-free" media growth was poor when methionine was the sole sulphur source, but maximal with cystine plus methionine. With regard to the inhibitory effect of selenite broth on the growth of *Salm. cholerae suis* it was observed that pentathionate had an outstanding neutralizing action on this whereas cystine alone had little, and methionine had no effect at all; a combination of these two SH-groups had a moderate effect but was not comparable to that of pentathionate. The sulphur metabolism of the organisms concerned is discussed.

[This is a paper of considerable interest but it is unfortunate that although there were observed differences in the reactions of the 7 strains of *Salm. cholerae suis* examined there was no indication of which of these were *kunzendorf* varieties. The question of $H_2S$ production might have some particular importance here.] *H. J. Bensted*

KAUFFMANN, F. **On the Biochemical Behaviour of New** *Salmonella* **Species (II).** *Acta Path. et Microb. Scandinavica.* 1959, v. 45, No. 4, 401–5.

With few exceptions strains of salmonella produce acid and gas from glucose and also ferment maltose, mannitol and sorbitol; they do not ferment lactose, sucrose, salicin or adonitol. Indole is not produced; they are able to use glucose or citrate as carbon source; they reduce nitrates but do not hydrolyse urea; they are MR +, VP − and KCN −.

In the fermentation of arabinose, xylose, rhamnose, trehalose, inositol, dulcitol and glycerol, in the production of $H_2S$ (in Kauffmann's medium), hydrolysis of gelatin and in ability to use organic acids, the different serotypes may differ.

This paper is mainly a table giving the different reactions of more than 80 new serotypes (here referred to as species). *S. T. Cowan*

SCHÄFLER, S. & MINTZER, Leonie. **Acquisition of Lactose-Fermenting Properties by Salmonellae. I. Interrelationship between the Fermentation of Cellobiose and Lactose.** *J. Bacteriology.* 1959, Aug., v. 78, No. 2, 159–63.

56 strains of salmonella were tested for their ability to ferment lactose after 2 passages in a partially defined medium containing cellobiose. Lactose fermentation was observed for a period of 40 days. 55 of the strains tested acquired the ability to ferment lactose after a period which varied according to each strain.

The stability of the lactose fermenting variants was tested after 20 passages in broth. Some strains of salmonella remained unchanged, some produced 2 types of lactose-fermenting colonies, and others dissociated into lactose-positive and lactose-negative colonies. However, lactose-positive colonies prevailed in most strains. The stability of cellobiose fermentation was marked even in lactose-negative variants and after 20 passages in broth.

It is suggested that the acquired ability to ferment lactose takes place in 2 stages, *viz.*:—

(1) A preliminary stage of cellobiose fermentation by part of the bacterial population.

(2) Fermentation of lactose by part of the cellobiose-positive population.

The lactose-positive variants often acquired the capacity to ferment arbutin and salicin. This may be due to steric similarity between the $\beta$-galactosidic bond

of lactose and the β-glucosidic bond of cellobiose, arbutin, and salicin. *May F. McCallum*

TINELLI, R. & STAUB, A. M. Étude chimique des polyosides somatiques des *Salmonella*. III.—Oxydation périodique de polyosides extraits de différentes *Salmonella*. **[Chemical Study of Somatic Polysaccharides of Salmonellae. III. Periodic Oxidation of Polysaccharides Extracted from Different Salmonellae]** *Bull. Soc. Chimie Biol.* 1959, v. 41, Nos. 9/10, 1221–31, 2 figs. [20 refs.]

EDSALL, G., CARLSON, Margaret C., FORMAL, S. B. & BENENSON, A. S. **Laboratory Tests of Typhoid Vaccines used in a Controlled Field Study.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1017–32. [19 refs.]

Most readers will be familiar with the field studies with different typhoid vaccines carried out in Yugoslavia in 1954–55, the findings of which were reported by CVJETANOVIC [this *Bulletin*, 1957, v. 32, 836] and the YUGOSLAV TYPHOID COMMISSION (*Bull. World Health Organization*, 1957, v. 16, 897). The laboratory tests in connexion with these studies were carried out jointly at the Walter Reed Army Institute of Research, Washington, DC, U.S.A.; the Lister Institute of Preventive Medicine, Elstree, England, and the Central Institute of Hygiene, Zagreb, Yugoslavia. This report is concerned with the work done at the Walter Reed Institute. Full details are given of the materials used and the techniques employed, together the results of the serological, active and passive mouse protection tests with the 2 test vaccines—alcohol-treated and heat-killed phenol-preserved respectively—used in the trial, and the Walter Reed Institute control vaccines. An analysis of the data obtained, depending upon which set of findings is selected, permits any one of the following conclusions:

1. The active-immunization tests in mice, with either saline or mucin challenges, and a 6-day interval between vaccination and challenge, clearly indicate that the alcohol vaccine is the more potent. So also do the passive-protection tests with the saline challenge and the Vi-agglutinin titres obtained in rabbits.

2. The passive-protection test with the mucin challenge and the O-agglutinin titres in rabbits, indicate that there is no significant difference in potency between the two vaccines. The active-immunization test with mucin challenge at 14 days is suggestive of the same conclusion.

3. The H-agglutinin titres induced in rabbits indicate that the phenol vaccine is superior to the alcohol vaccine.

The significance of these conflicting findings remains to be determined. The results of the field trials themselves as reported by the Yugoslav Typhoid Commission provided evidence that the phenol vaccine protected against typhoid fever in man whereas no such evidence was provided by the alcohol vaccine. The suggestion that H antibodies induced by the phenol vaccine may, after all, have some connexion with the protective value observed with this vaccine is difficult to accept on the basis of H antibodies alone.

Whatever may emerge from further studies of this very important and interesting subject, which are clearly indicated, it must be concluded from the report of the trial itself and the results presented in this paper that the vaccine which possessed the higher Vi-antigen content gave less protection against typhoid fever in man than the vaccine possessing little of this antigen.

*H. J. Bensted*

FISEK, N. H., GÖREN, S. & AKYAY, N. **Mouse Challenge with *Salmonella typhosa* T 5501 in testing the Potency of Typhoid Vaccine.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1257–9.

[It has been customary ever since the introduction of the typhoid mouse protection test (active and passive), which was before the Vi antigen had been identified, to employ mouse virulent cultures for the challenge. The early studies in this field appeared to establish the fact that the mouse virulence of a typhoid bacillus was directly proportional to the Vi-antigen content of that particular strain or culture. In all the tests undertaken at that time there was a wide difference in the mouse virulence of Vi-positive and Vi-negative cultures and since there are always obvious disadvantages in all animal protection tests in using a challenge of low virulence, high virulence cultures became the rule for the challenge in these protection experiments. Although it is accepted that the Vi antigen is of prime importance in protecting the mouse against challenge with *Salmonella typhi* the position of the Vi antigen in the natural infection of man has in recent years been seriously questioned. Field trials have strongly suggested that typhoid vaccines deficient in Vi antigen are actually more protective than vaccines in which the Vi antigen is fully preserved [see above] and this has greatly complicated the laboratory assessment of the efficiency of the prophylactic vaccines now in use.

During an examination of a number of Vi-negative strains of typhoid bacilli STANDFAST (in press) found that certain of these cultures had a mouse virulence not outside the order of the virulence of Vi-positive strains. One of these Vi-negative strains, T 5501, the mouse LD50 of which was about one-tenth of that of the classical non-Vi strain, O 901, was passed to the present authors by Standfast and this paper describes experiments undertaken to show that this strain is suitable as a mouse challenge in comparing the protective values of alcohol- and phenol-treated typhoid vaccines.

While it is clear from personal conversations with Standfast that strain T 5501 possesses peculiar properties it would be preferable, before considering further this paper, to await the publication of Standfast's own paper.] *H. J. Bensted*

VELAUDAPILLAI, T. **Phage-Typing of S. Virchow.** *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 146, No. 1, 84–8. [18 refs.]

GULASEKHARAM, J., VELAUDAPILLAI, T. & NADARAJAH, K. N. **Salmonella Angoda: a New *Salmonella*.** *Indian J. Med. Res.* 1959, Sept., v. 47, No. 5, 484–6.

"A new salmonella type with the antigenic formula 30:k:enx was isolated from a stool of a case of

diarrhoea in Ceylon. It was named *S. angoda* as the patient was from the Fever Hospital, Angoda, in the district of Colombo."

JUENKER, A. P. & BILANOW, Helen. **New *Salmonella* Type: Salmonella Detroit.** *J. Bacteriology.* 1959, Oct., v. 78, No. 4, 599.

The formula is 42:z-1,(5).

SEN, R. **Transaminases in *Shigellae*.** [Correspondence.] *Nature.* 1959, Aug. 29, v. 184, Suppl. No. 10, 741.

WU, Kai-Yu & CHENG, Kuo-Kuei. **[On Haemagglutination Test with "O" Antigen of the *Shigella* Group]** *Acta Microbiologica Sinica.* 1959, May, v. 7, Nos. 1/2, 82–7. [12 refs.] [In Chinese.]

The English summary appended to the paper is as follows:—

"The sensitizing antigen was prepared from 18–24 hours growth on agar which was washed off with sterilized and buffered normal saline. The supernatant fluid and the sediment were separately collected to serve as the antigen. Original dilution of the sediment contains 2.0 billion bacteria per ml., and this dilution was maintained up to the actual test. Human or animal red cells were sensitized with serial dilution of the above antigen. On performing the actual tests, antibody dilution method was employed.

"As a result of our experiments, HA test showed its superiority over ordinary agglutination reaction in being more sensitive and more specific. The sensitivity, in terms of titres of the immune sera, has been raised 8–16 fold, and type specificity as well as group specificity has been demonstrated.

"Regarding the sensitizing ability, no material difference had been observed between the supernatant and the sediment. It was considered that at least a portion of the antigen is water soluble and all thermostable. Boiling of the antigens for two hours is essential.

"All four groups of human erythrocytes can be employed instead of 'O' group alone. However, if unknown sera are to be tested against known antigen, 'O' cells should be used in order to avoid false positive reaction. Red blood corpuscles of rabbit, of guinea pig and of chicken have been found to serve our purpose. A final suspension of 0.25% of red blood cells is the optimum concentration."

WU, Kai-Yu & CHENG, Kuo-Kuei. **[Application of Haemagglutination Test in the Diagnosis of Bacillary Dysentery]** *Acta Microbiologica Sinica.* 1959, May, v. 7, Nos. 1/2, 88–93. [10 refs.] [In Chinese.]

The English summary appended to the paper is as follows:—

"The diagnosis of bacillary dysentery, acute or chronic, can hardly be said to be established until it is confirmed bacteriologically. However, the bacteriological procedure is expensive and time consuming. In recent years, direct rapid agglutination and precipitation tests have been tried by Soviet workers and found to be more sensitive but less specific.

"In this laboratory, a series of experiments have been performed employing boiled saline extract from 18–24 hours whole stool culture as the sensitizing agent for human 'O' group of erythrocytes to be agglutinated by known immune sera.

"On the first experiment, conventional bacteriological culture method and the HA were carried out simultaneously on 311 stool specimens collected from acute cases of dysentery. Later, direct rapid agglutination was made in addition to the above two tests on 100 stool cultures. The test has been found to be more sensitive and highly specific, as it gave 10–15% more positive reactions. The majority of the positive reactions occurred in high dilutions of immune sera with the titres of 1:640 and even 1:10240. The results of the HA and bacteriological method agreed in 74% of the 311 specimens tested, and showed a discrepancy of about 26%. Among the latter group, 15.8% were negative by bacteriological culture method but positive by a HA and about 7% were on the reverse.

"A few strains from 107 strains of colon and paracolon bacilli isolated from healthy children exhibited cross HA reaction toward Flexner and Sonne immune sera, but in lower titres.

"From the above results, the HA test is found to be sensitive and specific and therefore it may serve as a supplementary test for the routine diagnosis of bacillary dysentery."

OLINICI, N. & GOREA, A. Toxicitatea tulpinilor de *Shigella disenteriae* I (B. Shiga) si reacţia de precipitare în gel. **[Toxicity of *Shigella dysenteriae* I Strains and the Gel-Precipitation Test]** *Microbiol., Parazitol., Epidemiol.* Bucharest. 1959, May–June, v. 4, No. 3, 219–24, 2 figs.

The English summary appended to the paper is as follows:—

"The gel-test applied in the selection of exotoxigenous strains of *b. Shiga* did not yield the same results as titration *in vivo* except in *R* strains. Exotoxigenous *S* strains gave but few flocculation bands. Dysenteric exotoxin displays 2 flocculation bands which are almost constant, and a series of secondary bands. Sera of horses immunized for a long period display a greater number of bands than sera of recently immunized ones. Reactions in gels do not take place with weak sera and toxins. They take place only with fresh sera collected no longer than 4 months before performance of the test. Formaldehyde prevents flocculation. *S* and *R* strains of *b. Schmitz* and *Sonne* and their chloroform extracts give flocculation bands with antitoxic *Shiga* serum. The gel-test appears to be useful in the detection of antigenic interrelation."

LABREC, E. H., FORMAL, S. B. & SCHNEIDER, H. **Serological Identification of *Shigella flexneri* by means of Fluorescent Antibody.** *J. Bacteriology.* 1959, Sept., v. 78, No. 3, 384–91, 3 figs. [13 refs.]

Flexner rabbit antisera, unabsorbed or highly absorbed type-specific and sheep anti-rabbit globulin

were conjugated either with fluorescein isocyanate or fluorescein isothiocyanate, mainly the latter [this *Bulletin*, 1959, v. 34, 299]. The cultures used were either standard strains or strains properly identified by orthodox methods. The fluorescein labelled antisera or globulin fractions were maximally diluted to the point where each still stained strongly its homologous antigen. When labelled unabsorbed sera were used there were the expected cross-staining reactions; these appeared to be more marked with antibody containing Flexner group factors 3, 4 & 6 than with antibody to the group factors 7, 8 or 9. When, however, the labelled highly absorbed type sera were used there were practically no cross-staining reactions with smears of 18-hour Flexner cultures and the reaction could be regarded as specific.

Attempts were made to apply the method for the examination of stools of experimentally infected guineapigs, but owing to the considerable amount of non-specific staining the results could not be regarded as satisfactory. In view of the possibility of interference by shared antigens among the Enterobacteriaceae it would seem unlikely that the method would prove to be a reliable procedure for the exact identification of bacterial types in smears of natural dysenteric exudates. The orthodox serological identification of dysentery bacilli is usually a very simple and rapid procedure and, interesting as this new technique is, it does not appear to offer any advantage over the established methods. *H. J. Bensted*

Iosub, C., Bercovici, C., Beşleagă, V., Sechter, I., Weinfeld, M. & Beldiman, I. Considerații asupra tulpinilor de *Sh. flexneri* tip 6 izolate în Moldavia. [**Remarks on Type 6 *Sh. flexneri* Strains isolated in Moldavia**] *Microbiol. Parazitol., Epidemiol.* Bucharest. 1959, May–June, v. 4, No. 3, 225–9.

The English summary appended to the paper is as follows:—

"The authors report the biochemical, antigenic, and bacteriophage properties of 29 strains of type 6 *Sh. flexneri* (B. Newcastle) isolated in Moldavia; these are the first strains of dysenteric bacilli of this type to be isolated in this country. Their initial identification was performed on the basis of the characteristic bacteriophage spectrum and of the presence of the surface antigen which prevents agglutination with polyvalent Flexner serum.

"Based on the bacteriophage spectrum and the presence of the surface antigen, the authors agree with the views of Soviet workers who differentiate the Newcastle bacillus from *Sh. flexneri* and consider it to be an intermediate type between the latter and *Sh. boydi*."

Serény, B. **Acquired Natural Immunity following Recovery from Keratoconjunctivitis Shigellosa.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 292–305. [19 refs.]

Guineapigs infected by the installation into 1 eye of cultures of Flexner bacilli are found, on recovery, to have developed a local non-specific tissue immunity of some significance. The opposite, spared, eye shows a low grade immunity which is type-specific in accordance with the particular strain of Flexner employed to produce the keratoconjunctivitis. The blood serum of the recovered guineapigs contains low level type-specific agglutinins and mouse protecting antibodies, as demonstrated in the passive mouse protection test.

[A very similar article by the same author, in which the findings were identical appeared in the Hungarian journal *Acta Microbiologica*, 1958, v. 5, 343 [see this *Bulletin*, 1959, v. 34, 673] and it would appear that this is a further example of 2 different journals reporting a communication delivered at an International Congress.]

[See also *ibid.*, 1958, v. 33, 690; 1959, v. 34, 567.] *H. J. Bensted*

Joó, I., Pusztai, S. & Csizmás, L. Immunobiologische Untersuchungen mit Dextran-Präparaten an Darmbakterien. II. Aktive und passive Schutzversuche. [**The Effects of Dextran Preparations on Intestinal Bacteria. II. Active and Passive Immunization**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, May, v. 117, No. 5, 386–400, 5 figs. [34 refs.]

Many tables with corresponding figures are set out to show the protective effects of various vaccines for typhoid and dysentery infection in mice.

The results of injections, as infecting dose, of large numbers of bacteria are compared with those obtained with much smaller numbers suspended in 2% dextran solution.

The results were related to the size of the immunizing dose of vaccine in a more satisfactory way with the small infecting dose suspended in dextran and this is attributed to the exclusion in a large measure of the toxic effects associated with the greater numbers of bacteria required to produce a lethal effect in the absence of some substance which decreases resistance.

Dextran, mucin and zymosan, all polysaccharide preparations have this capacity to decrease resistance and for Pillemer and his school [see this *Bulletin*, 1956, v. 31, 226] it is to be attributed to the effect which they have in diminishing the properdin content of the blood. The difficulty of relating observations of this kind to the protective value of these vaccines in man is discussed.

[For Part I, see this *Bulletin*, 1958, v. 33, 606.] *J. W. McLeod*

Straka, R. P. & Stokes, J. L. **Metabolic Injury to Bacteria at Low Temperatures.** *J. Bacteriology.* 1959, Aug., v. 78, No. 2, 181–5. [13 refs.]

During prolonged storage at low temperatures many species of bacteria may slowly die. In the process of dying they exhibit different degrees of sub-lethal injury, which may in some degree be characterized and assessed by ascertaining the extent to which the bacteria have become more exacting in their nutritional requirements. Various strains of *Escherichia coli* and of several *Pseudomonas* species were tested in this way. The injured cells, which might comprise 40% of a bacterial population, were no longer able to grow on a simple glucose-salts agar but required a rich complex trypticase soy agar. On such a medium, and in certain fractions of

it, the bacteria could recover from certain degrees of metabolic injury. In promoting recovery, the common growth factors appeared to be ruled out but there was some evidence that specific peptides were active.

*J. W. Howie*

ELIN, V. L. [**A Contribution to the Biology of** *Bacillus coli* **Commune**] *Mikrobiologiya.* Moscow. 1957, v. 26, No. 1, 17–21. [In Russian.]

The English summary appended to the paper is as follows:—

"1. Bacillus coli commune is able to multiply in physiological saline with no additional nutrition.

"2. The requisite carbon, nitrogen, sulphur, iron and other elements are apparently derived from air. Besides $CO_2$ and nitrogen, the air probably contains volatile compounds of sulphur, iron, phosphorus etc. which are assimilated by the bacillus.

"3. The aerial mode of nutrition is not a result of adaptation to prolonged exposure to physiological saline, but is inherent to the microbe as one of its primitive capacities.

"4. The above fact sheds some light upon the properties of the primitive forms of life, their mode of assimilation, and opens vast prospects for studying the biochemistry of microbes.

"5. Further inquiry is required into the aerial mode of assimilation with respect to other microbes cultivated in physiological saline."

MUSCHEL, L. H. & OSAWA, E. **Human Blood Group Substance B and** *Escherichia coli* **O86.** *Proc. Soc. Exper. Biol. & Med.* 1959, Aug.–Sept., v. 101, No. 4, 614–17. [15 refs.]

It was found that decomplemented high titre human anti-B serum had some temporary inhibitory effect on the growth of *Escherichia coli* O 86 and it has also been shown that group A substance is active against the Vi antigen. A considerable number of bacterial and viral species together with some toxoids were examined with anti-A and anti-B sera. There was anti-A activity with the Vi antigen containing bacteria such as the typhoid bacillus, the coliform Ballerup and the particular strain of *Escherichia coli* 5396/38 which is very rich in Vi antigen but the effect was not consistently reproduced. Group B activity was found only in 5 strains of *E. coli* and all these strains were O type 86. The organisms tested included a range of coli O types, salmonellae, shigellae, vibrios, staphylococci, corynebacteria and leptospires. In addition rickettsiae, examples of the lymphogranuloma-psittacosis group and a number of neurotropic viruses were also tested. The significance of these observations is by no means clear at present. The apparent relationship between human blood group substance B and *E. coli* O 86 suggested a possible association between blood groups and infective disease, but the fact that the effect of anti-B serum is restricted to a single coli type and the group A activity to an antigen which recent work indicates is not of importance in human disease does not support this view. It is possible that further work on the subject may clarify the position.

*H. J. Bensted*

EGGLESTON, L. V. & KREBS, H. A. **Permeability of** *Escherichia coli* **to Ribose and Ribose Nucleotides.** *Biochem. J.* 1959, Oct., v. 73, No. 2, 264–70, 1 fig. [26 refs.]

SCHWINCK, Ilse & ADAMS, E. **Aromatic Biosynthesis. XVI. Aromatization of Prephenic Acid to *p*-Hydroxyphenylpyruvic Acid, a Step in Tyrosine Biosynthesis in** *Escherichia coli.* *Biochim. et Biophys. Acta.* 1959, Nov., v. 36, No. 1, 102–17, 4 figs. [23 refs.]

GOLDSTEIN, A., GOLDSTEIN, Dora B., BROWN, Beverly J. & CHOU, Shao-Chia. **Amino Acid Starvation in an** *Escherichia coli* **Auxotroph. I. Effects on Protein and Nucleic Acid Synthesis and on Cell Division.** *Biochim. et Biophys. Acta.* 1959, Nov., v. 36, No. 1, 163–72, 3 figs. [12 refs.]

DRAKULIC, M. **Ribonucleic Acid Metabolism in U.V.-Irradiated** *Escherichia coli* **B.** *Biochim. et Biophys. Acta.* 1959, Nov., v. 36, No. 1, 172–6, 1 fig. [15 refs.]

HEDEGAARD, J., MASPERO-SEGRE, Silvia, THOAI, N. v. & ROCHE, J. Influence de l'histidine et de ses métabolites sur la biosynthèse des purines par *Escherichia coli* B. V. Mode d'action dans des cultures inhibées par l'azasérine. [**Influence of Histidine and its Metabolites on the Biosynthesis of Purines by** *Escherichia coli* **B. V. Mode of Action in Cultures Inhibited by Azaserin**] *C.R. Soc. Biol.* 1959, v. 153, No. 6, 954–9, 1 fig. [11 refs.]

MILLER, S. & BOND, T. J. **Factors affecting the Biosynthesis of Folinic Acid by** *Escherichia coli.* *J. Bacteriology.* 1959, Oct., v. 78, No. 4, 488–91.

HERRMANN, W. Klebsiellen als Erreger von Meningitis bei Frühgeborenen und Kleinstkindern. [*Klebsiella* **as Cause of Meningitis in Mature and Premature Infants**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 384–90.

A small epidemic of purulent meningitis was observed in the first half of 1958 in a clinic for infants. There were 7 cases all fatal.

The *Klebsiella* isolated were identified as capsule type 2 by Dr. KAUFFMANN.

The author, however, deplores the extremely exacting investigations required for such typing which are beyond the capacity of most laboratories on the scale required for epidemiological investigations. A scheme of identification as one or other of the main types is suggested:

(1) The normal and ubiquitous type produces acid in agar containing ammonium salts and glucose but alkali if sodium citrate is substituted.

(2) A pathogenic type which produces acid in both media, and

(3) A pulmonary type which does not cause change of reaction in either medium.

An interesting practical point is that the infants who developed this infection had all been given heat-sterilized human milk. Those fed with unsterilized human milk escaped. *J. W. McLeod*

NIKONOV, A. G., YEVSEYEVA, V. I., BIBIKOVA, P. D. & BICHUL', K. G. **Cultivation of *Vibrio comma* in the Small Intestine of Guinea-pigs.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 12, 1925–7. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 122.]

JENKIN, C. R. & ROWLEY, D. **Toxic Proteins from *Vibrio cholerae* and Water Vibrios which are Lethal for Mice.** *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 191–202, 1 fig. [19 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 123.]

MUKERJEE, S., GUHA, ROY, U. K., GUHA, D. K. & RUDRA, B. C. **Studies on Typing of *Vibrio cholerae* by Bacteriophage. Part II: Further Observations with Strains from Calcutta Epidemics.** *Ann. Biochem. & Exper. Med.* Calcutta. 1959, May, v. 19, No. 5, 115–24, 3 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 122.]

OUCHTERLONY, Ö. **A Selective Medium for isolating Cholera Vibrios.** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No. 3, 274–84. [15 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 121.]

STINEBRING, W. R. & KESSEL, R. **Continuous Growth of *Brucella abortus* in Mononuclear Phagocytes of Rats and Guinea Pigs.** *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 412–15, 1 fig. [10 refs.]

This work was undertaken in order to determine whether it was possible to maintain continuous growth of *Brucella abortus* by serial passage in mammalian mononuclear cells in tissue culture procedures. Rat and guineapig mononuclear cells were obtained by first injecting saline intraperitoneally and 2 days later washing out the peritoneum with Hanks balanced salt solution. Washed mononuclear cells in a concentration of $1 \times 10^7$/ml. were mixed with $2{\cdot}5 \times 10^8$ brucella cells in 5 ml. of 30% autologous serum in Hanks medium. This mixture was transferred to suitable containers and incubated for 2 hours. The mononuclear cells ingesting the brucella cells attached themselves to the floor of the culture flasks. The supernate was decanted and replaced with the identical medium supplemented with 10 μgm. streptomycin/ml. The extracellular brucella cells were killed, but those within the mononuclear cells remained viable. After 3 days the tissue culture was washed gently with warm Hanks solution to remove the residual streptomycin and debris. Further Hanks solution was added and this constituted a complete cycle which could be repeated again and again where the culture process was successful.

Smooth cultures of *Br. abortus* were successfully carried through guineapig mononuclear tissue culture as a continuous operation, but rough cultures failed to survive. On the other hand mononuclear cells from the adult rat did not provide the same suitable conditions and continuous intracellular growth of the organism in rat mononuclear cell tissue culture was not observed.

*H. J. Bensted*

WUNDT, W. Untersuchungen über die Antigenstruktur von Intermediärstämmen aus der Gattung *Brucella.* [**Investigation of the Antigenic Composition of Intermediate Strains of *Brucella***] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 145, No. 6, 543–55. [10 refs.]

The existence of strains of *Brucella* which give the specific cultural reaction of *Br. abortus* but agglutinate with monospecific (absorbed) *melitensis* sera or the reversed picture is already well recognized. The author has attempted by saturation with graded amounts of bacterial suspension to establish the proportions in which the A (*abortus*) and M (*melitensis*) antigens are present in these "intermediate" strains. He concludes that the less frequent strains of *abortus* cultural type but *melitensis* agglutination are ones which contain less *abortus* antigen than the typical *melitensis* strains.

The more common "intermediate" which is biochemically a *melitensis* strain but agglutinates with *abortus* monospecific serum, contains more M antigens than *abortus* or *suis* types but less than *melitensis* types.

*J. W. McLeod*

JACOTOT, H. & VALLÉE, A., with the technical collaboration of A. LE PRIOL. Étude expérimentale d'une souche vaccinale de brucelle dérivée de la souche B19 (souche Zdrodovsky). [**Experimental Study of a Vaccine Strain of *Brucella* derived from the B19 (Zrodovsky) Strain**] *Ann. Inst. Pasteur.* 1959, May, v. 96, No. 5, 638–41.

A strain of *Brucella* designated BA [this *Bulletin*, 1956, v. 31, 1101] and used extensively in the U.S.S.R. and Poland to protect personnel exposed to bovine brucellosis in the course of their occupation has been investigated. This strain, derived from the parent strain B19 by subculture in media containing bile, differs from the latter in culture by giving viscous films of growth on agar and a glutinous deposit in broth whereas growths of the rough mutants of the parent strain on agar are dry.

This BA strain produces a septicaemia of short duration and lesser intensity in the guineapig than actively virulent strains. This notwithstanding, it proved an efficient antigen in the protection of rats, both as live vaccine and dead, and gave considerable although less complete protection to guineapigs. The BA strain is peculiarly liable to the S-R mutation. *J. W. McLeod*

GUERRA, M. L'infezione brucellare del coniglio: aspetti batteriologici e sierologici. [**Bacteriological and Serological Aspects of Brucellosis in Rabbits**] *Giorn. di Malattie Infettive e Parassit.* 1959, Aug., v. 11, No. 8, 717–22.

24 rabbits of an average weight of 2,500 gm. were divided into 4 groups and inoculated intravenously with $6{\cdot}5 \times 10^9$ and $6{\cdot}5 \times 10^8$ *Brucella melitensis* 16m strain and $3{\cdot}4 \times 10^9$ and $3{\cdot}4 \times 10^8$ *Br. abortus* 544 strain respectively. Bacteraemia was limited and of short duration, falling off very markedly by the 7th day, while blood cultures taken 15 and 30 days later remained sterile in all cases. Agglutinin titrations and complement-fixation tests always became positive in 15 days and remained so throughout the period of observation, 3 animals in each group being killed after 3 months and 3 after 6 months. Both reactions fell off with time.

In some sera, but only among those taken more than a month after infection, the complement-fixation test gave the paradoxical finding of a negative result at 1 in 8 and 1 in 16 and a positive result (no haemolysis) beyond that. This happened more often with *Br. melitensis* than with *Br. abortus* antigen and did not occur if 4 or 8 antigen units in 0·2 ml. were used instead of 2 units. These findings probably depended on the effects of optimal proportion between reagents. Screening tests at 1 in 8 only may perhaps lead to false negatives.

In some rabbits infection was shown to persist for at least 6 months, generally in those showing fairly high agglutinin and complement-fixation titres. In rabbits killed after 3 months no macroscopic lesions were present and micro-organisms were isolated in small numbers. Animals killed after 6 months with positive cultural results showed hyperplasia of the abdominal lymph glands or, more rarely, foci of caseous lesions in the organs. This occurred with *Br. melitensis* but not with *Br. abortus*. Infection in rabbits is therefore of a chronic character and can persist in lymph glands while other organs tend to sterilize themselves. The infected rabbit can appear quite healthy, a fact of epidemiological importance. *E. Agius*

BRADLEY, G. Mary & SPINK, W. W. **Acute Hepatic Necrosis induced by *Brucella* Infection in Hyperthyroid Mice.** *J. Exper. Med.* 1959, Nov. 1, v. 110, No. 5, 791–800, 8 figs. on 4 pls. [17 refs.]

SCHMIDT, J. Über *Pasteurella pseudotuberculosis*-Infektionen des Menschen. [*Pasturella pseudotuberculosis* **Infection in Man**] *Arch. f. Hyg. u. Bakt.* 1959, June, v. 143, No. 4, 262–86, 3 figs. [38 refs.]

An account is given of 9 cases of human infection with *Pasturella pseudotuberculosis*, 8 of which concerned children aged 8–16 years. The onset was usually acute, with abdominal pain and pyrexia; the disease was diagnosed as acute or subacute appendicitis in 8 cases, and 7 patients were subjected to laparotomy. The correct diagnosis was established by agglutination tests and in one case isolation of the causative organism from lymph nodes removed at operation. *D. J. Bauer*

SWARTZ, M. N. & KUNZ, L. J. ***Pasteurella multocida* Infections in Man. Report of Two Cases—Meningitis and Infected Cat Bite.** *New England J. of Med.* 1959, Oct. 29, v. 261, No. 18, 889–93. [34 refs.]

CAVANAUGH, D. C. & RANDALL, R. **The Role of Multiplication of *Pasteurella pestis* in Mononuclear Phagocytes in the Pathogenesis of Flea-Borne Plague.** *J. Immunology.* 1959, Oct., v. 83, No. 4, 348–63, 9 figs. [16 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 119.]

WINTER, Carrie C.; MOODY, M. D. **Rapid Identification of *Pasteurella pestis* with Fluorescent Antibody. I. Production of Specific Antiserum with Whole Cell *Pasteurella pestis* Antigen** [WINTER & MOODY]. *J. Infect. Dis.* 1959, May–June, v. 104, No. 3, 274–80. [20 refs.] **II. Specific Identification of *Pasteurella pestis* in Dried Smears** [WINTER & MOODY]. *Ibid.*, 281–7, 3 figs. [10 refs.] **III. Staining *Pasteurella pestis* in Tissue Impression Smears** [MOODY & WINTER]. *Ibid.*, 288–94, 1 fig. [19 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 120.]

ALBRINK, W. S. & GOODLOW, R. J. **Experimental Inhalation Anthrax in the Chimpanzee.** *Amer. J. Path.* 1959, Sept.–Oct., v. 35, No. 5, 1055–65, 6 coloured figs. on pl.

4 young chimpanzees were exposed to aerosols containing *Bacillus anthracis* spores, the estimated number of spores inhaled ranging from 32,000 to 66,500. Each animal developed a bacteraemia within 2–3 days which, in 2 cases, progressed until the animals died on the sixth day after exposure. Bacteraemia persisted at a low level for 8 days in the 2 survivors.

On re-exposure to larger doses (90,300 and 112,000 spores) both survivors developed a delayed bacteraemia which was of short duration in one animal but progressed in the other until death on the 8th day after exposure.

Post-mortem findings indicated that *B. anthracis*, administered by the respiratory route causes a fulminating septicaemia rather than a localized pulmonary infection. There were no tracheal or bronchial lesions as seen in wool-sorters' disease in man. *John R. Norris*

COX, R., SOCKWELL, G. & LANDERS, B. ***Bacillus subtilis* Septicemia. Report of a Case and Review of the Literature.** *New England J. of Med.* 1959, Oct. 29, v. 261, No. 18, 894–6, 1 fig. [16 refs.]

SHEN, S. C., HONG, M. M. & BRAUNSTEIN, A. E. **The Main Path of Nitrogen Assimilation in *Bacillus subtilis*.** *Biochim. et Biophys. Acta.* 1959, Nov., v. 36, No. 1, 290–91.

WILLIS, A. T. & HOBBS, G. **Some New Media for the Isolation and Identification of Clostridia.** *J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 511–21, 9 coloured figs. on 2 pls.

The authors have found that the best rapid differentiation among the clostridia is obtained by the use of 2 media. These are 12% nutrient gelatin with 1% glucose added on a basis of brain/heart infusion with phenol red as indicator. Evidence of fermentation of glucose was obtained on adding phenol red and the presence of gelatinase was also determined on this medium.

The second medium was lactose-egg-yolk-milk agar [see also this *Bulletin*, 1958, v. 33, 887]. 400 ml. of an agar medium containing approximately 1% lactose and 1·3 ml. of a 1% solution of neutral red with a basis of meat infusion broth were mixed with 15 ml. of egg yolk suspension and 60 ml. sterile milk. This medium provided evidence of Nagler effect, if the surface of one half were treated with antitoxin; there was also evidence of clearing by proteolysis of the opacity due to the milk and of fermentation of lactose. The appearances of growth on plates of the lactose-egg-yolk-agar are illustrated by colour plates. [Some of these are not very convincing.]

The value of the addition of 250 μgm. of neomycin per ml. of medium [this *Bulletin*, 1956, v. 31, 676; 1959, v. 34, 285] was confirmed. *J. W. McLeod*

MURRAY, T. J. **Survival of *Clostridium tetani*.** *J. Bacteriology.* 1959, Aug., v. 78, No. 2, 293–4.

At the end of a study of the thermal resistance of spores of *Clostridium tetani* between 1927 and 1930, the 34 strains of *Cl. tetani* used were inoculated into brain heart infusion medium solidified with 1·8% agar and the tubes were sealed with a blast lamp.

Early in 1959 some of the contents of each tube were transferred to brain heart infusion plus 0·1% agar and incubated. 25 strains developed typical anaerobic growth in 24 hours, 5 in 48 hours and 1 each in 3 and 5 days. The remaining 2 strains failed to grow initially, but did so when cultures were made from a second and third tube respectively. Typical Gram-positive rods with "drumstick" spores were found. There was strain variation in the number and time of appearance of the spores.

Evidently these 34 strains were viable and capable of typical growth and sporulation after 29 years in sealed tubes of brain heart agar. *H. J. O'D. Burke-Gaffney*

RAYNAUD, M., TURPIN, A., RELYVELD, E. H., CORVAZIER, R. & GIRARD, O. Préparation d'antitoxine antitétanique par immunisation des chevaux avec des anatoxines tétaniques de haute pureté. [**Preparation of Tetanus Antitoxin by Hyperimmunization of Horses with a Purified Toxoid**] *Ann. Inst. Pasteur.* 1959, June, v. 96, No. 6, 649–58, 3 text figs. & 9 figs. on 3 pls. [42 refs.]

This article is illustrated by photographs of gel diffusion lines of precipitation obtained by the method of OAKLEY and FULTHORPE [this *Bulletin*, 1953, v. 28, 656] and also by those derived from observations on immunoelectrophoresis. The conclusions reached are that when purified anatoxin is used for immunization a sharp single line is the only one observed by the gel diffusion method till late in the course of immunization. It is also shown that a normal horse, immunized for the first time may yield a serum with low L+/Lf. ratio which is of low avidity. Such a serum may be relatively rich in gamma globulin.

The immunization of horses, starting with basic immunity, tends to give sera with a high and maximal L+/Lf. ratio about the end of a month which appears when the ration of beta to gamma globulin is already high.

It would seem, therefore, that the antitoxin of avid character may be associated as much or more with the beta than with the gamma globulin contrary to some observations published on this subject [this *Bulletin*, 1954, v. 29, 109]. *J. W. McLeod*

LAMANNA, C. **The Most Poisonous Poison. What do we know about the Toxin of Botulism? What are the Problems to be solved?** *Science.* 1959, Sept. 25, v. 130, 763–72, 3 figs. [30 refs.]

This article surveys the activities of *Clostridium botulinum* and its toxins and includes sections on ecology, chemistry, immunity, physiology, pharmacology and prophylaxis. It is recognized that efforts have been largely concentrated on Type A toxin which when crystallized is described as a white odourless protein of high molecular weight and unknown taste containing 19 typical amino acids. Prepared batches of amorphous and crystalline material show constancy of biological activity and amino acid composition with an isoelectric point of 5·6 and a molecular weight of 900,000 dissociating above *p*H 6·5 into particles of molecular weight 40,000 to 100,000.

The haemagglutinin reactions of type A bacilli are described in detail; the toxic units are thought to be in association with the haemagglutinin units. Less than $0{\cdot}1 \times 10^{-3}$ microgramme of toxin causes death in mice and a dose 3,500 times larger is lethal for a man of 104 kgm. weight.

The toxins can be absorbed through thin layers of epithelial tissue and through abrasions and burns of the skin and mucous membrane; the small intestine is said to be the major site of systemic absorption. Evidence of toxicity may be detected in the intestinal contents and faeces for several days. The mechanism of poisoning is described and is said to be caused by specific interference with release of acetylcholine from the terminal ends of nerves.

Antitoxin and nontoxic, strongly immunogenic stable toxoids are readily produced.

This article should be read in its entirety.

*Betty C. Hobbs*

PRÉVOT, A. R. & SILLIOC, R. Activation de la toxinogénèse botulique D par *Bacillus licheniformis*. [**Activation of Toxigenesis of *Clostridium botulinum* Type D by *Bacillus licheniformis***] *Ann. Inst. Pasteur.* 1959, May, v. 96, No 5, 630–32.

With an inoculum from a portion of salted ham which had been the source of an outbreak of botulism in the vicinity of Lake Chad [this *Bulletin*, 1959, v. 34, 145],

it was possible to obtain toxin of potency of 300,000 MLD for the mouse. This culture was a mixed one containing *Clostridium botulinum* type D and the aerobe *Bacillus licheniformis*. When, however, the anaerobe was isolated in a state of purity it rapidly lost its toxigenic power as is the rule with strains of this type and artificial addition of *B. licheniformis* to the cultures of this atoxigenic strain failed to restore toxigenicity. Attempts to develop toxin from such cultures by the action of trypsin were also unsuccessful. In the latter respect the contrast with the results obtained with *Cl. botulinum* type E is interesting. *J. W. McLeod*

GRECZ, N., WAGENAAR, R. O. & DACK, G. M. **Inhibition of *Clostridium botulinum* by Culture Filtrates of *Brevibacterium linens*.** *J. Bacteriology*. 1959, Oct., v. 78, No. 4, 506–10, 1 fig. [11 refs.]

CAMPBELL, L. L., Jr. & WINIARSKI, W. **Isolation and Properties of a Subtilin Resistant Strain of *Clostridium botulinum*.** *Applied Microbiol.* Baltimore. 1959, Sept., v. 7, No. 5, 285–8, 1 fig. [18 refs.]

A subtilin-resistant strain of *Clostridium botulinum* was developed from spore suspensions of strain 62A by means of the dilution tube technique.

The resistant strain was isolated by the shake tube dilution method with Baltimore Biological Laboratory Eugonagar containing 100 μgm. per ml. subtilin. Resistance was maintained through the spore stage and could be demonstrated after 2 years in the absence of subtilin.

The resistant strain was found to be toxic for mice. It failed to sporulate well in the usual media although there was little difference between the sporulation of the resistant strain and its sensitive parent in beef heart medium containing granules of meat.

Resistance was not caused by an enzyme capable of inactivating subtilin; cross resistance to nisin was not demonstrated.

The use of subtilin combined with mild heat treatment to preserve low-acid canned foods is questioned in view of the ease with which stable subtilin-resistant strains of *Cl. botulinum* are produced; but subtilin could be used as a supplement to control spoilage of low-acid canned food by organisms resistant to heat processes designed to protect against *Cl. botulinum*.

*Betty C. Hobbs*

MEISEL, H., ALBRYCHT, H. & RYMKIEWICZ, D. **Comparative Investigations on Phospholipase C (Alpha Toxin) Content in Culture Fluids, Vegetative Cells and Spores of *Clostridium perfringens* Type A at Various Incubation Periods.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 10, 395–9.

BITTNER, J. Étude sur la toxinogénèse du vibrion septique. **[Study of Toxin Formation by *Clostridium septicum*]** *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.-Dec., v. 17, Nos. 3–4, 417–25, 1 fig. [16 refs.]

Strain 59 which originated in the U.S.A. and was obtained from Moscow was kept in subculture of Komkova medium-Pope broth with 0·4% gelatin, 0·5% glucose, 0·1% agar and minced meat under vaseline seal.

With 1% inoculua of this, the best medium for toxin production was found to be Martin peptic digest broth, heavily buffered with bi-potassium phosphate 2% and containing 0·2% of sodium pyruvate and 1% glucose. Incubation was for 22 hours at 37°C. The size of the vessel used seemed important and was possibly related to permitting a minimal access of oxygen to a fluid in which anaerobic growth could proceed. The conditions found to be associated with good toxin formation were active gas production, a fall in *p*H to about 6·5 and predominance of short bacillary forms.

The order of potency of the toxins obtained was 1300 MLD50 per ml. for the white mouse. *J. W. McLeod*

KRANZDORF, H. & BITTNER, J. Sur la méthode de préparation de l'anatoxine du vibrion septique purifée, concentrée et adsorbée sur phosphate d'aluminium. **[A Method of Preparation, Purification, Concentration and Adsorption on Aluminium Phosphate of a *Clostridium septicum* Toxoid]** *Arch. Roumaines Path. Exper. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 427–33.

Direct formalinization of *Clostridium septicum* toxin yields a product which kills the mouse on account of a non-specific anaphylactoid component. This difficulty is best surmounted by a preliminary concentration and purification of the crude toxin by acid precipitation in 2 stages. The first stage is carried out at *p*H 4·6–4·8 and the second precipitate is obtained from the supernatant by bringing it to *p*H 3·0–3·2. Acidification is with 0·2% metaphosphoric acid, the final *p*H levels being obtained with N/1 $H_2SO_4$ or the whole procedure can be carried out with trichloracetic acid.

The products obtained by either method are very similar in concentration and antigenic efficiency. On an average the titre of such products is 56 Lf./mgm. N.

The final detoxification is with 0·1% formaldehyde for 3–4 days at 37°C. *J. W. McLeod*

ADDAMIANO, Laura. Classificazione serologica di alcuni ceppi di leptospire provenienti dall'Indonesia. **[Serological Classification of Certain Strains of Leptospires Isolated in Indonesia]** *Rendiconti Istituto Superiore di Sanità*. Rome. 1959, v. 22, Pt. 1, 5–12. English summary (9 lines).

Agglutination and cross-absorption tests showed that strain Bindjei [which was received at the Istituto Superiore di Sanità in 1938 labelled *L. pyrogenes*] was in fact the "complete" (AB) subserotype of *Leptospira canicola*. The author suggests that it should be regarded as the type strain of the subserotype since the Anvers strain, which VAN RIEL [*Tropical Diseases Bulletin*, 1947, v. 44, 320] also found to be the "complete" subserotype of *L. canicola*, has since been lost.

[The rest of this article reports the results of tests to "tidy up" the identities of various other strains which proved to be wrongly designated. The detailed protocols cannot be summarized and are in fact chiefly of interest

to laboratories which maintain cultures of type strains for distribution. The discrepancies revealed re-emphasize the absolute necessity for the regular and strict serological control of all " type " strains. It may be appropriate to mention that the WHO/FAO Leptospirosis Study Group is collaborating in the production of a series of standard antisera prepared against all the officially recognized serotypes of leptospires, and that these antisera will eventually be available for distribution to national reference laboratories, together with cultures of the type strains.] *J. C. Broom*

BRAUN, O. H. Zur Methodik der quantitativen Analyse der Darmflora. **[Technical Problems in the Quantitative Analysis of Intestinal Micro-Organisms]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 390–401, 1 fig. [27 refs.]

The methods recommended for this purpose by HAENEL and his collaborators [this *Bulletin*, 1959, v. 34, 146] are discussed. A good deal of this does not convey much except to those familiar with the media and methods in common use in German laboratories.

The most interesting point raised is the relative values of different media for the cultivation of the anaerobic lactobacillus—*L. bifidus*. A number of media containing tomato juice, yeast extract and peptic digest of casein have been recommended but the author has found the defined but complex medium of TOMARELLI *et al.* (*J. Biol. Chem.*, 1949, v. 181, 879) to be the best. The formula for this is given.

A medium containing human milk has been compared with the others and, although it does not give over all a better result, there are a number of *L. bifidus* strains which grow only on it.

To make good this defect in the Tomarelli medium, an oligosaccharide ($\beta$-ethyl N acetyl-glucosaminide) has been added which it has been claimed can take the place of the " bifidus factor " in human milk.

The greatest discrepancy between proportions of bacteria staining Gram-positive and Gram-negative respectively as determined by direct observation and by culture occurs with adult stools and is attributed tentatively to failure to grow the micro-organisms of the " *Bacteroides* " group. *J. W. McLeod*

## RICKETTSIAE

STOENNER, H. G., HOLDENRIED, R., LACKMAN, D. & ORSBORN, J. S., Jr. **The Occurrence of *Coxiella burneti*, *Brucella*, and other Pathogens among Fauna of the Great Salt Lake Desert in Utah.** *Amer. J. Trop. Med. & Hyg.* 1959, Sept., v. 8, No. 5, 590–96. [13 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 114.]

YU, En-Shu & WU, Hsien-Yi. **[Further Study on the Different Types of *Trombicula deliensis* and Transovarian Transmission of *Rickettsia orientalis*]** *Acta Microbiologica Sinica.* 1959, May, v. 7, Nos. 1/2, 10–15. [In Chinese.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 113.]

KAWAMURA, A., NISHIOKA, K., AIKAWA, K. & TAKAGI, T. **Persistent Infection of *Rickettsia orientalis* (Ozeki Strain) in Ehrlich Ascites Carcinoma Cells and Effect of ED Virus upon this Host-Parasite Relationship.** *Japanese J. Exper. Med.* 1959, June, v. 29, No. 3, 167–79, 4 figs. [13 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 24.]

## BACTERIOPHAGES

NOJIMA, T. & FUKUMI, H. **Final Products in the Abortive Infection of T2 Bacteriophage in the Mutant $(B/2)_5$ of *E. coli*, Strain B.** *Japanese J. Med. Sci. & Biol.* 1959, Apr., v. 12, Nos. 1/2, 9–24, 5 text figs. & 27 figs. on 6 pls.

In this instance of abortive infection of an *Escherichia coli* B mutant by phage T2, it had previously been shown that phage DNA, recognized by its hydroxymethyl cytosine, and phage head protein, recognized by its complement-fixing activity, were both formed [this *Bulletin*, 1958, v. 33, 185]. The infected cells lysed, although few infective particles were formed. This paper reports that the lysate had a host killing effect, far greater than could be accounted for by any mature particles contained, and that the bacteria thus prevented from forming colonies no longer supported the multiplication of intact phage. In electron micrographs, particles similar to " doughnuts ", the empty head found in proflavine lysates, were seen, and in some cases the heads appeared to have tail-like appendages, occasionally looking like tail cores without their sheaths.

*Janice Taverne*

SHUG, A. L., FRASER, D. & MAHLER, H. R. **Studies in Partially Resolved Bacteriophage-Host Systems. V. A possible Role of a Polyribonucleotide in the Infection of *E. coli* B with Bacteriophage T2.** *Biochim. et Biophys. Acta.* 1959, Nov., v. 36, No. 1, 142–57, 1 fig. [30 refs.]

ROTHSTEIN, E. L., MANSON, L. A., HARTZELL, R., Jr. & KRITCHEVSKY, D. **Effects of Deuterium Oxide on the Synthesis of *T5* and *T7* Bacteriophages.** [Correspondence.] *Nature.* 1959, Oct. 10, v. 184, Suppl. No. 15, 1167–8. [10 refs.]

DIRKX, J. Relations entre la fixation d'un bactériophage et l'état physico-chimique de la surface bactérienne. **[Relationships between the Fixation of a Phage and the Physico-Chemical State of the Bacterial Surface]** *Ann. Inst. Pasteur.* 1959, Oct., v. 97, No. 4, 526–48, 12 figs. [24 refs.]

Previous work had shown that the flocculating properties of *Shigella flexneri* F6 and the adsorption of phage to the bacteria at different ionic strengths could be predicted by colloid theory in the case of rough (R) bacteria, but not for smooth (S) bacteria [DIRKX *et al.*, *Biochim. Biophys. Acta.*, 1958, v. 27, 442; this *Bulletin*, 1958, v. 33, 399]. The anomalous behaviour of the S strain was explained, however, by postulating the existence of a mechanical obstacle to adsorption which covers the surface of the cell.

To obtain further information about this hypothetical barrier, viscosity measurements were made on cultures of R and S bacteria at different ionic strengths. Again, a difference was found between the strains. With the S strain, a drop in specific viscosity was observed as small numbers of cations were added to the medium. This behaviour is typical of hydrophil colloids, and is caused by the contraction of the molecules which accompanies the lessening of the electrostatic repulsion between ionized groups. Specific viscosity was found to increase linearly with bacterial concentration, except at lower concentrations when the curve departed from linearity, more markedly with cultures of S than of R bacteria.

On the basis of the finding that the viscosity of S cultures is greatest at low ionic strengths, the author suggests the following explanation of observations on phage adsorption to S strains: At low ionic strengths the macromolecules on the bacterial surface are extended in long, charged chains which prevent the approach of phage particles. At higher ionic strengths the chains contract, possibly in the coils of a helix, forming a specific spatial configuration which provides the phage receptors. The S antigen may be the macromolecule in question. The author investigated the possibility that the long chains are identical with the fimbriae on the bacterial surface observed under the electron microscope by DUGUID and others [*e.g.* GILLIES & DUGUID, this *Bulletin*, 1959, v. 34, 672]. He concludes that they are similar but not identical, as fimbriae give rise to the same kind of anomalies as the S antigen, but to a greater degree. *Janice Taverne*

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## VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Enteric group; Arthropod-borne group; Others.**

BRITISH MED. BULL. 1959, Sept., v. 15, No. 3, 175–245, illustrated. [Numerous refs.] **Current Virus Research.**

The fruits of the great technical advances in virology are now beginning to be reaped. This is clearly demonstrated in the British Medical Bulletin devoted to current virus research. C. H. ANDREWES has gathered an excellent team of Commonwealth virologists and as a result has produced a series of authoritative and informative short articles on a wide range of virus topics of interest not only to the virologist but also to the epidemiologist and physician.

The first article is by F. M. BURNET on virus genetics (pp. 177–180). He outlines the technical requirements for genetic analysis of virus variation. Although viral genetics may never become of direct medical importance he stresses the role of genetic ideas in the elucidation of virus-host interactions at both the cellular and population levels. He notes that when virologists talk of virus attenuation or adaptation to new hosts all the evidence is that in reality "spontaneously" occurring mutants are being selected [perhaps future bulletins will be able to analyse this spontaneity]. Since mutation is a rare, random event it follows that virus stocks can be kept free of mutants by propagating them at high dilution.

J. C. N. WESTWOOD discusses the application of the tissue culture methods which are largely the cause of the present rapid rate of advance of virology (pp. 181–184). The importance of these techniques in diagnostic virology and epidemiology requires no emphasis. They have also been responsible for great advances in the knowledge of host-virus interactions, of the mode of action of antibody [as first foreshadowed by Andrewes, see this *Bulletin*, 1930, v. 5, 38] and in knowledge of the chemical nature of animal viruses. The possibility of using cell lines grown in continuous culture for preparing highly potent virus which after purification could be used in vaccines is mooted.

A. ISAACS and D. C. BURKE discuss their important discovery that heterologous interference by inactivated myxoviruses is mediated by a protein substance smaller than virus which is called interferon (pp. 185–188). Interferon is produced when inactive influenza virus is added to susceptible cells. Interferon appears to be a product of abortive virus infection of the cell and would seem to be a non-specific inhibitor of viruses imitating the range of heterologous interference induced by the inactive virus. Thus influenza interferon is active not only against influenza virus and other myxoviruses but also against the unrelated vaccinia virus and some arbor viruses. It seems that interferon production may be responsible for some of the chronic infections of tissue culture cells where healthy cells and virus persist together. If the virus is partially inactivated at 37°C. such inactive virus induces interferon production and

preserves the cells. Recently Ho and ENDERS have shown (*Proc. Nat. Acad. Sci.*, Washington, 1959, v. 45, 385 [to be abstracted in the succeeding issue of this *Bulletin*]) that a substance similar to interferon is produced when human kidney cells are infected with a chick-adapted type 2 poliovirus which does not cause a visible cytopathic effect in the kidney cells. The discovery of interferon is of great theoretical importance and it is hoped that it may be of value in the treatment or prevention of virus diseases.

D. A. J. TYRRELL and H. G. KLEMPERER discuss the value of new techniques for the study of virus multiplication (pp. 189–192). These include phase contrast microscopy of viable cells, staining for RNA and DNA and for virus antigen with fluorescent antibody. They also describe how modern techniques of biochemistry with radioisotopes, antimetabolites and cell fractionation, are increasing knowledge of the chemical events leading to virus multiplication.

G. BELYAVIN discusses the application of immunological techniques (pp. 193–196). He first considers direct flocculation of viruses by antisera which can be demonstrated in a fluid medium in a tube or in agar gel. This simple and, until recently, neglected technique may be of increasing importance in virus diagnosis and serological analysis. Haemadsorption, immune adherence and fluorescent antibody techniques are also described.

A. W. DOWNIE (pp. 197–200) reviews the knowledge of chickenpox and zoster which is rapidly increasing since the demonstration of WELLER and STODDARD [this *Bulletin*, 1952, v. 27, 894] that the virus could be grown and propagated regularly *in vitro*. The serological identity of the 2 viruses seems undoubted and it is possible that chickenpox and zoster are primary and secondary manifestations of the same virus infection analogous to primary and recurrent manifestation of herpes simplex infection.

Measles is discussed by K. MCCARTHY (pp. 201–204). It appears probable that only 1 serological type of measles virus exists and that this causes not only measles but also giant-cell pneumonia. It is now possible to titrate the measles antibody content of human gamma globulin used for prophylaxis and to prepare a vaccine (attenuated) for active immunization.

Vaccination against poliomyelitis in the United Kingdom is considered by G. W. A. DICK and D. S. DANE (pp. 205–209). They conclude that potent killed vaccine is very effective but that much vaccine now being prepared is not sufficiently potent. Live vaccines are thought to pose serious difficulties of control because of their capacity to spread, and the hazard of reversion to virulence of such spreading excreted virus. They also make a plea for assessing living vaccines on their performance rather than by analogy with yellow fever vaccine. They point out that the duration of immunity following smallpox vaccination or TN type 2 attenuated poliovirus infection is not very long.

A. D. MACRAE discusses the enteroviruses which comprise polio, ECHO and Coxsackie viruses (pp. 210–215). These are grouped together because they are isolated from the human alimentary canal, have a similar size and are ether-resistant. A useful table shows the range of clinical manifestation from paralysis to abacterial meningitis, fever and a rash, herpangina, pleurodynia, diarrhoea, myocarditis (and pericarditis) often fatal in the newborn, and finally mild respiratory infections.

Influenza and its complications are discussed by C. H. STUART-HARRIS (pp. 216–220). The threat of another pandemic like that of 1918 still overshadows all work on influenza. Notwithstanding the great advances in the virology of influenza, the Asian influenza epidemic revealed that, despite feverish efforts to make vaccine, virologists can do no more than predict an epidemic and analyse its effects.

C. H. ANDREWES discusses the common cold and new respiratory viruses (pp. 221–224). This is a valuable attempt to produce order out of incipient chaos. The various new myxoviruses, ECHO virus and miscellaneous viruses are listed and briefly discussed. The common cold virus or viruses are still elusive and the importance of other factors, notably falling humidity, in evoking catarrhal symptoms after infection with cold viruses, are mentioned.

H. G. PEREIRA (pp. 225–230) deals with adenoviruses, which are not only important causes of epidemic respiratory and eye diseases of young adults, but also valuable tools for investigating the nature of viruses. A striking electronmicrograph showing the external structure of adenovirus particles by HORNE *et al.* (*J. Molecular Biol.*, 1959, v. 1, 84) is shown.

L. H. COLLIER reviews the important new work on trachoma and blennorrhoea in which he has played a prominent part (pp. 231–234). These agents can now be readily isolated in the yolk sac under the cover of large doses of streptomycin (20,000 units per ml.). The great advances which have been made promise to bring the scourge of trachoma under control.

Arboviruses (C. E. GORDON SMITH, pp. 235–239) are very important medically in some parts of the world and to those interested in the complex factors involved in virus evolution. There are now known to be about 79 distinct arboviruses. The last paper is by F. FENNER (pp. 240–245), who discusses myxomatosis, giving a most interesting summary of the changes in virus virulence and host resistance following release of myxomatosis in Australia. The virus has become more attenuated and the rabbits genetically more resistant. Both more virulent and more attenuated strains reinoculated into wild rabbits where myxomatosis was endemic were eliminated by the endemic strain. It was found that an attenuated strain produced severe lesions in animals held in a cold environment and very rare lesions in animals kept warm (70°F. for 12 hours, 92–95°F. for 12 hours).

*A. J. Beale*

MAY, G. Zur Verwendung von Caseinhydrolysat als Nährmedium für Gewebekulturen. [**Casein Hydrolysate as a Nutrient Medium for Tissue Cultures**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 7/8, 481–4.

A 5% stock solution of casein hydrolysate (Bayer, Leverkusen; Merck, Darmstadt) is prepared in Hanks solution without bicarbonate, and is stored at −20°C. until required. The tissue culture nutrient medium recommended by the author consists of 100 cc. 5% casein hydrolysate solution, 800 cc. Hanks solution and 100 cc. calf serum. The *p*H is adjusted to 7·2 with 7·5%

sodium bicarbonate solution at room temperature; the medium is then sterilized by filtration, and can be stored at 4°C. for 8–14 days. Penicillin and streptomycin are added before use, and also 100 units of muronal per cc. when amnion cultures are being prepared. The medium gave good growth of HeLa, FL, KB, monkey and pig kidney and human amnion cells, and titres of 7·4–8·75 log units were obtained in HeLa and amnion cells grown in the medium and infected with poliomyelitis virus.

*D. J. Bauer*

BLAKEY, B. R. & GIFFORD, G. E. **Discarded Blood Bank Blood as a Source of Protein for Cultivation of HeLa Cells.** [Correspondence.] *Nature.* 1959, Oct. 10, v. 184, Suppl. No. 15, 1158.

ISAACS, A. & WESTWOOD, Marguerite A. **Inhibition by Interferon of the Growth of Vaccinia Virus in the Rabbit Skin.** *Lancet.* 1959, Sept. 12, 324–5, 1 fig.

The authors describe experiments with interferon which show that this substance is able to prevent the infection of rabbit skin by large doses of vaccinia virus only if the interferon is given the day before the virus. Protection against small doses of virus was complete when it was given before or at the same time as the virus. Interferon given after inoculation of virus had no effect. When the interferon was diluted $\frac{1}{3}$, the vaccinial lesion was attenuated, but not completely suppressed.

Interferon produced in rabbit cells was effective in rabbits, but interferon produced in chick embryo cells was only slightly so. Contrariwise, interferon from chick embryo cells, but not from rabbit cells, protected chick embryo cells.

[See also this *Bulletin*, 1958, v. 33, 188.]

*Colin Kaplan*

ISAACS, A. **Action of Interferon on the Growth of Sublethally Irradiated Virus.** *Virology.* New York. 1959, Sept., v. 9, No. 1, 56–61.

Influenza (MEL) and fowl plague viruses sublethally irradiated with ultra-violet light were shown to be more sensitive to the action of interferon than the corresponding unirradiated viruses. Both unirradiated and irradiated viruses were used in low multiplicities which eliminated the possible occurrence of auto-interference or multiplicity reactivation. The findings suggest that sublethal irradiation of the virus reduced its chance of multiplying in interferon-treated but not in normal cells. Two possible and not mutually exclusive explanations for these findings are offered. The first is that irradiation damage to the virus can be repaired in normal but not in interferon-treated cells. The second is that the cells are conditioned to produce interferon rather than virus either by pretreatment with interferon or by the use of irradiated virus.

*H. G. Pereira*

HENLE, W., HENLE, Gertrude, DEINHARDT, F. & BERGS, V. V. **Studies on Persistent Infections of Tissue Cultures. IV. Evidence for the Production of Interferon in MCN Cells by Myxoviruses.** *J. Exper. Med.* 1959, Oct. 1, v. 110, No. 4, 525–41. [13 refs.]

The authors have previously shown that infection of certain human cell lines by Newcastle disease (NDV), mumps and haemadsorption type 1 viruses renders the cells resistant to the action of several cytopathic viruses [Henle *et al.*, this *Bulletin*, 1959, v. 34, 392]. This resistance was shown to be due to interference [Bergs *et al.*, *ibid.*, 393] but the number of resistant cells greatly exceeded that of cells yielding virus [Deinhardt *et al.*, *ibid.*, 393]. It is shown in the present report that the interference observed in this investigation is mediated by interferon.

Production of interferon is demonstrated in MCN cultures inoculated with ultraviolet-irradiated mumps, NDV, influenza A and Sendai viruses. Interferon was similarly produced in primary cultures of human kidney, rabbit kidney and mouse fibroblasts but not in HeLa cells.

Interferon was detected in MCN cultures infected with mumps virus and it is suggested that it may play an important role in the establishment and maintenance of persistent virus infections.

*H. G. Pereira*

CONSTABLE, F. L. **Psittacosis Elementary Bodies.** [Correspondence.] *Nature.* 1959, Aug. 8, v. 184, Suppl. No. 7, 473–4, 1 fig.

The author claims that electron microscopy of mature psittacosis lesions on the chorio-allantoic membrane of 8- to 10-day chick membranes reveals two distinct types of elementary body. These differ in size, one being 0·25 to 0·3 $\mu$, the other 0·4 to 0·5 $\mu$ in diameter.

The smaller is electron dense, with a thick layer of dense material immediately beneath the outer limiting membrane, this layer being separated from a dense central mass by a clearer zone.

The larger form shows a layer of granular material beneath the limiting membrane which merges gradually with a diffuse granular central zone, becoming increasingly less dense towards the centre.

The relative number of these two forms is more or less equal. The possibility that they represent different developmental stages is being investigated.

*S. P. Bedson*

SANNA, A., ANGELILLO, B. & PISANO, E. Ulteriori ricerche sul 'esistenza di relazioni antigeniche fra i virus del gruppo linfogranuloma-psittacosi e quello del tracoma. [**Further Researches on the Existence of Antigenic Relations between the Viruses of the Lymphogranuloma-Psittacosis Group and of Trachoma**] *Igiene Moderna.* 1959, May–June, v. 52, Nos. 5/6, 415–21. [11 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 181.]

SOLOVIEV, V. D. & MASTYUKOVA, Y. N. **A Study of the Immunogenicity of Smallpox Vaccines.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1099–110.

After killing a large number of rabbits by intracerebral injection of neurovaccine challenge, the authors of this paper showed that the protective antigenicity of

smallpox vaccines is proportional to their infectivity. [See COCKBURN *et al.*, this *Bulletin*, 1957, v. 32, 725; and CROSS *et al.*, *ibid.*, 1959, v. 34, 17.] They also showed (without killing the test animals) that antigenicity was inversely proportional to the intensity of reaction provoked by intradermal or intratesticular challenge with testis-adapted vaccinia virus. There is also a suggestion that virulence [undefined] is associated with immunogenicity. [The table purporting to show this shows that (a) rabbits vary in their responses and (b) 1 LD50 cannot be relied upon to kill.] *Colin Kaplan*

POWELL, W. F. **Radiosensitivity as an Index of Herpes Simplex Virus Development.** *Virology*. New York. 1959, Sept., v. 9, No. 1, 1–19, 6 figs. [31 refs.]

These experiments were done with the HRE strain of herpes simplex virus, growing in the L strain of mouse fibroblasts. Growth curves for intracellular and extracellular virus were first obtained. Experiments of the Luria-Latarjet type were then done by subjecting infected cells to X-rays and UV light at intervals after infection, and plotting virus survival curves.

The sensitivity of infected cells to inactivation by X-rays increased rapidly during the first hour of infection, reaching a maximum of 11 times that of free virus by the end of the eclipse phase. A similar phenomenon was observed with UV light. During the last half of the eclipse phase stabilization to UV light occurred, without any change in X-ray sensitivity. Inactivation curves during the first 3 hours of infection could be resolved into 2 single-hit curves, suggesting that there were 2 types of infected cell. The capacity curve resembled those described for other animal viruses. The observation that heavily irradiated cells could give rise to infectious virus was confirmed. No evidence of genetic homology between virus and host cell was found in "rescue" experiments in which irradiated free virus was adsorbed to normal and irradiated cells before plating.

Inactivation of free virus by UV light of different wave lengths indicated that the light was absorbed by a nucleo-protein, of which the most light sensitive part was protein. *Janice Taverne*

ADA, G. L., LIND, Patricia E., LARKIN, Lois & BURNET, F. M. **Failure to recover Infective "Ribonucleic Acid" from Myxovirus Preparations.** [Correspondence.] *Nature*. 1959, Aug. 1, v. 184, Suppl. No. 6, 360–61.

Infective ribonucleic acid (RNA) has been recovered from many animal viruses by phenol treatment of crude virus preparations. Influenza virus is known to contain RNA, in about the same amount per particle as does poliomyelitis virus and some plant viruses. However, no product infective for mouse brain or chick embryo could be recovered from high titred stocks of 3 strains of influenza A, influenza B or Newcastle disease virus after phenol treatment. Phenol treatment of purified virus did not extract all the RNA.

No recombinants were obtained in mixed infection experiments with RNA extracted from the WSE strain of influenza A and intact MEL or WS strains.

*Janice Taverne*

WHEELOCK, E. F. & TAMM, I. **Mitosis and Division in HeLa Cells infected with Influenza or Newcastle Disease Virus.** *Virology*. New York. 1959, Aug., v. 8, No. 4, 532–6, 12 figs.

HeLa cells induced to divide parasynchronously by chilling were infected with influenza (NWS) or Newcastle disease virus (NDV) and examined by the fluorescent antibody technique at the time when mitotic activity was expected to be maximal. Dividing cells containing NWS or NDV antigens were observed in cultures infected 7 to 10 hours before mitosis. Division of cells infected with NDV was also observed by direct microscopical examination. *H. G. Pereira*

SMORODINTZEV, A. A., ALEXANDROVA, G. J., LOUSANINA, T. J., MOROZENKO, M. A. & SELIVANOV, A. A. Particularités virlogiques et sérologiques de la grippe pandémique de 1957. [**Virological and Serological Characteristics of the 1957 Influenza Epidemic**] *Ann. Inst. Pasteur*. 1959, Sept., v. 97, No. 3, 385–97, 3 figs.

Attempts to isolate Asian influenza (A2) virus from patients observed during the 1957 epidemic gave positive results in proportions varying from 50 to 75% in different localities. The strains were readily isolated in fertile eggs inoculated by the amniotic route and reached high haemagglutination and infectivity titres after a few egg passages. A small proportion of freshly isolated strains showed some pathogenicity for mice but this property was gradually lost with successive mouse passages in spite of high virus titres being reached in mouse lungs. Many egg adapted strains were shown to remain pathogenic for man. Avid and non-avid virus strains were distinguished by high or low sensitivity to thermolabile serum inhibitors respectively. Complement-fixing antigens common to A, A1 and A2 influenza viruses were demonstrated. The A2 strains were clearly distinguished from types A and A1 in haemagglutination-inhibition tests. A comparison between complement-fixation and haemagglutination-inhibition tests for the diagnosis of influenza revealed a higher sensitivity of the former. The results of haemagglutination-inhibition tests could be improved by the use of human group O red cells, non-avid virus strains and prolonged incubation of serum-virus mixtures before addition of red cell suspension.

Evidence is presented suggesting that the insensitivity of non-avid strains to serum inhibitors or antibodies is due to a stronger virus affinity for fowl cells than for antibody or inhibitor. *H. G. Pereira*

CHOPPIN, P. W. & TAMM, I. **Two Kinds of Particles with Contrasting Properties in Influenza A Virus Strains from the 1957 Pandemic.** [Correspondence.] *Virology*. New York. 1959, Aug., v. 8, No. 4, 539–42.

Limit-dilution allantoic passages of Asian influenza virus strains in the absence or presence of normal horse serum gave rise to inhibitor-sensitive and insensitive

variants respectively. It is suggested that differences in sensitivity of Asian strains to inhibitors is due to their varying content of sensitive and insensitive virus particles.

*H. G. Pereira*

BARUA, D. & FAUCONNIER, B. Élution non enzymatique du virus grippal. [**Non-Enzymatic Elution of Influenza Virus**] *Ann. Inst. Pasteur.* 1959, Oct., v. 97, No. 4, 479–96. [17 refs.]

Elution of influenza virus from chicken red cells is shown to result from 2 different mechanisms: (a) enzymatic elution characterized by ion and temperature dependence, by a slow and progressive course and by the irreversible destruction of cell receptors; (b) non-enzymatic elution, which occurs in the absence of ions (as shown by the use of formalin-treated red cells), rapidly reaching completion both at 37°C. and at 4°C. with slow and partial destruction of cell receptors. Elution of indicator virus (heated B-Lee) from formalin-treated red cells suspended in distilled water, takes place both at 37°C. and at 4°C.

*H. G. Pereira*

FRASER, K. B. **A Rapid Method of detecting Recombination between Inactivated and Infectious Preparations of Influenza A Virus.** [Correspondence.] *Virology.* New York. 1959, Aug., v. 8, No. 4, 544–6.

Recombination between heat-inactivated NWS strain and infectious MEL strain of influenza viruses was observed after the inoculation of equivalent amounts of the 2 virus preparations into the chorio-allantois of 12-day-old chick embryos. Detection of recombinants was greatly facilitated by the use of a mixed inoculum containing inactivated egg pathogenic strain and an infectious non-pathogenic strain. Reactivation was revealed by the appearance of haemorrhagic lesions characteristic of the inactivated strain. The reactivated virus appeared in the recombinant (N-M) form. Ether-treated NWS could not be reactivated by similar methods.

*H. G. Pereira*

FAUCONNIER, B. Variation naturelle du virus grippal de type A vis-à-vis des inhibiteurs sériques des animaux normaux. [**Spontaneous Variation of type A Influenza Virus towards Serum Inhibitors of Normal Animals**] *Ann. Inst. Pasteur.* 1959, Sept., v. 97, No. 3, 377–84, 2 figs. [16 refs.]

The sensitivity of 17 strains of influenza virus to normal serum inhibitors of different animal species (rabbit, mouse, fowl, pig, ox, sheep, guineapig, horse and monkey) is reported. The virus strains investigated included types A (3 strains), A1 (6 strains), A2 (1 strain), B (6 strains) and D (1 strain). The A strains are sensitive only to rabbit and pig sera. Strains A1 are mainly sensitive to ox and sheep serum inhibitors with one exception (strain Baratt, isolated in 1947) which, like the A2 strain, is sensitive to guineapig, fowl, horse and pig inhibitors. The B strains were not sensitive to any of the inhibitors tested and the D strain was only slightly inhibited by guineapig serum.

Heat-treatment of the sera (60°C. for 1 hour) caused a reduction of inhibiting activity against all but the A2 virus.

It is suggested that normal serum inhibitors may play some part in the epidemiology of influenza.

*H. G. Pereira*

FAUCONNIER, B., LARTITÉGUI, R. M. & BARUA, D. Adaptation artificielle du virus grippal aux inhibiteurs du sérum normal. I.—Obtention, à partir d'une souche sensible, d'un variant insensible par culture du virus en présence de son inhibiteur. [**Experimental Adaptation of Influenza Virus to Inhibitors of Normal Sera. I.—Isolation of a Non-Sensitive Variant by Cultivation of the Sensitive Strain in the Presence of its Inhibitor**] *Ann. Inst. Pasteur.* 1959, Oct., v. 97, No. 4, 473–8. [13 refs.]

Influenza A-prime strains FM1 and D48 were serially propagated in fertile eggs in the presence of sub-neutralizing doses of normal bovine serum. This procedure resulted in a gradual diminution of virus sensitivity to the normal serum inhibitor. Virus obtained at progressive passage levels showed a gradual decrease in sensitivity to both the neutralizing and the haemagglutination-inhibiting activities of normal bovine serum.

*H. G. Pereira*

DRESCHER, J. Über Haemagglutinin- und Antikörper-Gehaltsbestimmungen. 5. Mitteilung. Untersuchungen über die Reaktion zwischen Virus und spezifisch die Hämagglutination hemmenden Antikörpern bei den Influenzavirusstämmen A'/Berlin/7/56 (Dutch), B/Berlin/2/55 und D/Sendai. [**The Determination of Haemagglutinin and Inhibiting Antibodies. 5th Communication: Investigations on the Reaction between Virus and Antibodies which specifically inhibit Haemagglutination with Influenza Virus Strains A-prime/Berlin/7/56(Dutch), B/Berlin/2/55 and D/Sendai**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 7/8, 485–504, 8 figs. [10 refs.]

In previous works [this *Bulletin*, 1958, v. 33, 406 *bis*; 1959, v. 34, 499, 1056] the author has described a photometric procedure for estimating influenza virus and inhibiting antibody, and has shown that the relation between the amount of virus and the amount of antibody fixed by it obeys the Freundlich adsorption isotherm, the constant of which is a characteristic parameter of the particular virus-antibody system. In the present work it is shown that the reactions between the A-prime/Berlin/7/56, B/Berlin/2/55 and D/Sendai strains of influenza virus and their corresponding inhibiting antibodies can also be described by the Freundlich adsorption isotherm, with characteristic constants for each strain, thus enabling the amount of antibody to be calculated from the values of the virus content before and after union with antibody. The paper contains a nomogram and numerical data which should be consulted in the original by those who wish to use the method.

*D. J. Bauer*

CLARKE, S. K. R. & SAYNOR, R. **Haemagglutination-Inhibition Tests against CA Virus.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 2, 288–94, 2 figs.

A survey of haemagglutination-inhibiting antibodies for croup-associated (CA) virus [this *Bulletin*, 1957, v. 32, 211; 1958, v. 33, 531] was carried out in Sheffield. Preliminary tests revealed the presence of non-specific CA virus inhibitors in human, monkey, calf, ferret and rabbit sera. These inhibitors could be destroyed by serum treatment with cholera vibrio filtrate. Virus inhibitors insensitive to cholera filtrate were found in normal guineapig serum. The proportion of human sera showing CA antibody rose steadily with age from none of 16 sera from babies under 1 year of age to 32 of 49 (65%) of sera from adults aged over 23 years. CA antibodies were found in 6 of 270 pairs of sera from patients with acute respiratory disease. *H. G. Pereira*

CRAMBLETT, H. G., KASEL, J. A. & UTZ, J. P. **Respiratory Illness in Children simultaneously infected with Hemadsorption Virus Type I and a Newly Recognized HeLa Enterovirus (HE).** *Pediatrics.* Springfield, Ill. 1959, Aug., v. 24, No. 2, 234–40, 1 fig. [10 refs.]

A cytopathic agent named HE virus (HeLa-enterovirus) was isolated in HeLa cell cultures inoculated with stools from 11 of 12 children observed during a hospital outbreak of acute respiratory illness characterized mainly by fever, conjunctivitis, rhinorrhoea, pharyngeal erythema and ronchi. Rises in HE virus neutralizing antibody were demonstrated in 7 of 8 patients from whom acute and convalescent sera were available. Rises in complement-fixing antibody for parainfluenza 3 virus (HA1) were also detected in 3 of 7 serum pairs, one of which also showed a rise in titre to parainfluenza 1 (HA2) virus. No antibody rises for influenza A, B and C or for adenovirus were observed. Parainfluenza 3 virus was isolated from the throat swab of 1 of the 12 patients but it is pointed out that the swabs had been stored at −20°C. for more than 2½ years. It is cautiously suggested that HE or parainfluenza viruses or both may have been responsible for the disease observed.

Some properties that connect the HE virus to the enterovirus group are presented [see also KASEL *et al.*, this *Bulletin*, 1959, v. 34, 587].

[The HE virus shares several properties with the Coe virus recently described by LENNETTE *et al.* (this *Bulletin*, 1959, v. 34, 397) but a serological comparison of these 2 agents has not so far been reported.] *H. G. Pereira*

BELL, S. D., Jr.; MCCOMB, Dorothy E.; MURRAY, E. S.; CHANG, Shih-Man; SNYDER, J. C.; FENG, Marie; SMITH, T. R. **Adenoviruses isolated from Saudi Arabia. I. Epidemiologic Features** [BELL, MCCOMB, MURRAY, CHANG & SNYDER] *Amer. J. Trop. Med. & Hyg.* 1959, July, v. 8, No. 4, 492–500, 1 fig. [17 refs.] **II. Pathogenicity of certain Strains for Man** [FENG, CHANG, SMITH & SNYDER]. *Ibid.*, 501–4.

I. The authors report the isolation of adenovirus from eye scrapings collected among a population of approximately 5,000 persons living in the Eastern Province of Saudi Arabia. The great majority of subjects investigated showed clinical signs of trachoma. 65 adenoviruses including types 3, 4, 6, 7, 8, 15, 16, 17, and 6 unnumbered types were isolated from 948 specimens. The viruses most commonly isolated were types 3, 8, 17 and strain BAR-2. 60 of the 65 viruses were isolated during the summer months of April to September. 90% of the viruses were isolated from children under 3 years and 81% from children under 2 years of age. No evidence was obtained of epidemics in any one area. A survey of adenovirus antibodies could not be carried out because of difficulties of obtaining blood samples. The possible role of adenoviruses in the aetiology of eye infections clinically diagnosed as trachoma is discussed.

II. Adenovirus strains isolated during the preceding study were tested for pathogenicity in 3 blind children. 3 virus strains belonging to types 16, 17 and an unnumbered type (designated strain 931) were each tested in 1 child at a dose of approximately 100 tissue culture ID50 inoculated into the conjunctival sac of each eye. Serological evidence of infection following inoculation was detected in all 3 children and confirmed by virus isolation in 2 children (strains type 16 and "931"). The 3 children showed clinical signs and symptoms compatible with a diagnosis of follicular conjunctivitis. Conjunctival scrapings from 2 cases of trachoma were similar inoculated to 2 additional blind children and gave rise to a disease clinically and histologically indistinguishable from the above adenovirus infection.

The children were aged 16, 17, 13, 7 and 8 years respectively. *H. G. Pereira*

FRIEDMAN, M. & DE BERRY, Patricia, with the technical assistance of W. L. BARRON. **Thermal Differentiation of the Adenovirus Complement Fixing Antigens.** *J. Immunology.* 1959, June, v. 82, No. 6, 535–41, 5 figs. [18 refs.]

Heat inactivation of adenovirus complement fixing antigens types 1 to 8 was shown to follow exponential curves. Inactivation rates at 68°, 70°, 73° and 75°C. varied according to the *p*H of the suspending medium. Antigens types 1, 2, 5 and 6 were increasingly heat sensitive as the *p*H varied from 6 to 8. The opposite was observed with antigens 3, 4, 7 and 8.

*H. G. Pereira*

DONALD, Heather B. & LIU, C. **Cytological Studies of Chick Embryo Cells infected with the Virus of Primary Atypical Pneumonia.** *Virology.* New York. 1959, Sept., v. 9, No. 1, 20–29, 3 figs. [11 refs.]

Chick embryos were infected with (Eaton's) virus of primary atypical pneumonia, and the bronchi later excised and stained with fluorescent antibody. Sections of bronchi showing the presence of virus antigen were examined under the electron microscope. Inclusion bodies were seen in the non-ciliated cells of the bronchial epithelium, but in no other cells. They are considered to be virus elementary bodies since they only occurred in tissues containing antigen, identified by fluorescence, and were never seen in uninfected embryos.

The particle diameter of 150–250 mμ agreed with Eaton's value obtained by filtration experiments [EATON *et al.*, this *Bulletin*, 1946, v. 21, 202].

The cytoplasm of the infected cells also contained numerous multilaminated structures. No other cell damage was seen. It is thought that the laminated structures represent injury to mitochondria caused by the virus. *Janice Taverne*

HOWES, D. W. **The Growth Cycle of Poliovirus in Cultured Cells. II. Maturation and Release of Virus in Suspended Cell Populations.** *Virology.* New York. 1959, Sept., v. 9, No. 1, 96–109, 3 figs. [12 refs.]. **III. The Asynchronous Response of HeLa Cells multiply infected with Type 1 Poliovirus.** *Ibid.*, 110–26, 4 figs. [12 refs.]

(ii) In previously reported studies [HOWES and MELNICK, this *Bulletin*, 1958, v. 33, 996] of the growth cycle of type 1 poliovirus in monolayers of monkey kidney cells it was found that poliovirus was present in the cell fraction and only slowly released into the supernatant fluid. The nature of this cell associated virus was investigated using cells in suspended culture. The experiments were carried out both with monkey kidney cells and also with ERK cells in suspended culture using relatively few cells per ml. and medium containing no inhibitors of virus. Using these precautions to minimise re-adsorption of virus that was released from cells or mechanical trapping of the virus in a monolayer of cells or the action of inhibitors in the medium, it was still found that cell associated virus accumulated in the early stages of virus growth and was only slowly released into the medium. This virus was almost certainly maturing in the cells since it was beyond the reach of antibody.

(iii) In the second paper using HeLa cells and ERK cells it was found that in individual cells virus matures in the cell and then is held for varying periods intracellularly and is subsequently released by a lysis-like process which takes approximately 1 hour. In a cell population due to asynchrony in the maturation phase and also in the intracellular retention time the results obtained show the summation of a series of overlapping phases. It is pointed out that this pattern of virus multiplication is similar to that observed with bacteriophage and dissimilar to that found with influenza virus where the process of maturation and release of virus proceed simultaneously. *A. J. Beale*

MURPHY, W. H., Jr. & ARMSTRONG, R. **Differentiation of Closely Related Cells by a Variant of Poliovirus, Type 2, MEF, Strain.** *J. Exper. Med.* 1959, Oct. 1, v. 110, No. 4, 629–42, 1 text fig. & 8 figs. on 2 pls. [27 refs.]

A strain of type 2 poliovirus (MEF1) obtained as a mouse brain suspension from Dr. Olitsky was found to produce a chronic infection in the HeLa cells maintained at the University of Minnesota. The cells were maintained in human or monkey serum containing no antibodies for type 2 poliovirus. The virus titre in the supernatant fluid was maintained through repeated serial passages of the cells; but the cells showed no cytopathic effect or variation in growth characteristics. Similarly the virus was unaltered. A variety of freshly trypsinized cells and cell lines were tested for their response to infection with the type 2 variant virus. They could be divided into 3 groups: (1) those supporting viral multiplication with complete cell destruction, *e.g.* monkey kidney, human amnion, HeLa cells (Hoye horse-serum-adapted line), Chang liver cells (parent line) and oesophageal cells (clone $A_2b$); (2) those supporting virus multiplication and showing areas of resistant cells, *e.g.* Chang's conjunctiva cells (clones $B_2A_2$, $B_2A_4$), oesophageal cells (parent), Chang's liver cells (clone $A_1A_1$) and Maben cells (parent); (3) cells that produce virus but show no visible cytopathic effects on the culture, *e.g.* HeLa cells (Minnesota origin parent and clone 4) and Chang liver cells (clone $D_1B_1$) and Chang's conjunctiva cells (parent).

It was found that some HeLa, Chang's conjunctiva, and liver cells were completely destroyed whereas other strains from other laboratories produced latently infected cultures.

2 cell lines, Maben and $D_1B_1$ liver cells, showed toxic degeneration after infection with large doses of poliovirus. Rapid passage of virus in latently infected cells in the hope of selecting cytopathic mutants were unsuccessful for the Minnesota HeLa cell line but were successful for the parent conjunctival cell line and $D_1B_1$ clone of liver cells. *A. J. Beale*

SPRUNT, Katherine, REDMAN, Winifred M. & ALEXANDER, Hattie E. **Infectious Ribonucleic Acid derived from Enteroviruses.** *Proc. Soc. Exper. Biol. & Med.* 1959, Aug.–Sept., v. 101, No. 4, 604–8.

The authors have previously described how it is possible to obtain RNA from poliovirus which produced plaques and intact poliovirus when used to infect susceptible cells (it also produces virus but not plaques on cells insusceptible to intact virus) [ALEXANDER *et al.*, this *Bulletin*, 1959, v. 34, 177]. They have now shown that the method of phenol extraction devised by GIERER and SCHRAMM (*Ztschr. f. Naturforsch.*, 1956, v. 11b, 138) yields infectious RNA from the following enteroviruses: a heat resistant mutant of Mahoney type 1 poliovirus, Coxsackie B4 and 5 (strains from patients), Coxsackie A7, and ECHO 1 and 8. The method of preparation was simple and can be achieved in an hour from tissue culture fluid containing 104 infectious particles. The infectivity of the RNA is only 1/1,000 or 1/10,000 of the intact virus preparations from which it is derived. *A. J. Beale*

DE SOMER, P., PRINZIE, A. & SCHONNE, E. **Infectivity of Polio Virus Ribonucleic Acid for Embryonated Eggs and Unsusceptible Cell Lines.** [Correspondence.] *Nature.* 1959, Aug. 22, v. 184, Suppl. No. 9, 652–3.

The authors have obtained infectious ribonucleic acid from the Mahoney strain of type 1 poliovirus by the method of GIERER and SCHRAMM (*Nature*, 1956, v. 177, 702) and found that this RNA gives rise to one cycle of growth after inoculation into the allantoic cavity of 8-day chick embryos. The virus produced in the allantoic fluid is not susceptible to ribonuclease and is more

resistant to heat than infectious RNA and unable to be maintained serially in eggs. All the evidence favours the idea that the RNA is capable of entering insusceptible cells and there going through a cycle of multiplication yielding intact, fully infectious poliovirus particles. Preliminary experiments suggest that not all insusceptible cells are capable of yielding intact poliovirus on infection with infectious RNA. A strain of rat tumour cells (DE7R), for example, failed to produce poliovirus on infection with poliovirus RNA. The authors have confirmed that infectious RNA is stabilized by the presence of 1 M sodium chloride which inhibits the activity of cellular ribonuclease [this *Bulletin*, 1958, v. 33, 533]. They find that the average yield of infectious RNA is about 0·01% of the titre of the intact virus from which it is derived.

[These observations provided independent confirmation for the work of HOLLAND *et al.* (this *Bulletin*, 1959, v. 34, 1193) and of MOUNTAIN and ALEXANDER (*ibid.*, 1960, v. 35, 91).] *A. J. Beale*

SMITH, W., BOISSARD, G. P. B., CHURCHER, Gillian M. & PARKER, Lesley. **Poliomyelitis-Virus Flocculation Reaction. Behaviour of Sera of Cases and Vaccinated Individuals.** *Lancet.* 1959, Oct. 17, 586–91. [15 refs.]

A study of the value of the poliovirus flocculation reaction previously described [SMITH *et al.*, this *Bulletin*, 1956, v. 31, 1172] for the serological diagnosis of poliomyelitis is described. It was found that the poliovirus flocculating antibodies appeared early in the course of the disease and declined early. Thus 80% of 41 cases showed flocculation antibody at a titre of 1/5 or higher in the acute serum against 73% in the convalescent sera. Indeed, in no case was a positive result obtained in the convalescent serum if the acute serum had been negative. It is suggested, therefore, that the presence of poliovirus flocculating antibodies in the acute phase of the disease may prove to be diagnostic. Heterotypic responses were sufficiently frequent to make the method unreliable from the point of view of specific type diagnosis. Another possible limitation to the method was revealed in a study of 50 sera from individuals given 2 doses of Salk-type vaccine and 18 sera from individuals given 3 doses. Nearly half of the vaccinated individuals developed flocculating antibodies after vaccination. The duration of these antibodies is as yet unknown. Comparisons between complement-fixing and neutralizing antibodies revealed that the flocculating antibodies are different from either of the other two.

The authors note that their results are somewhat different from those of SCHMIDT and LENNETTE [this *Bulletin*, 1959, v. 34, 1231]. These authors were able to observe rises in titre during convalescence and they also observed rather fewer heterotypic responses than is recorded in the present paper. The explanation for these differences is uncertain but one technical difference may be of great importance—the American workers incubated their virus-serum mixtures for 18 hours against the 4 hours used by Wilson Smith and his colleagues. The authors also point out that no separation in their analysis was made between the reactions of the D (intact) component and the C (degraded) component of poliovirus. The results of a comparison of the neutralizing and precipitating antibody response of 18 originally triple negative individuals to 3 doses of poliovaccine revealed the wide discrepancy between the two methods of antibody titration. It was also found that 8 of the 11 sera that gave rise to flocculating antibody had antibody to all 3 types. This suggests that the response to one type of antigen may cause a better response to the other types.

*A. J. Beale*

UEDA, T., TOYOSHIMA, S. & TSUJI, T. **The Effect of Alkylbenzenesulfonamide on Lansing Strain Virus in Mice.** *Keio J. of Med.* Tokyo. 1959, June, v. 8, No. 2, 57–64.

These authors claim to have shown that *p*-methylbenzene-phenylsulphonamide in a concentration of 500 μgm./ml. inactivates the Lansing strain of poliomyelitis virus *in vitro* in 1 hour, and that the same substance administered intravenously to mice 1, 2 or even 3 days after intracerebral inoculation with this virus reduces mortality from the infection. The LD50 was 44 mgm./kgm., and half this dose was more effective than lesser amounts when used therapeutically. [Consistent survival in treated animals and death in controls was never obtained: the widest difference is 23 survivors out of 30 in a treated group and 9 out of 30 in a control.] *L. P. Garrod*

NIKOLITSCH, M. & FENJE, P. Der Weg von der Peripherie aus inokulierten lymphocytären Chorio-Meningitis-Virus. [**Spread from the Periphery of Lymphocytic Choriomeningitis Virus after Inoculation**] *Arch. f. Hyg. u. Bakt.* 1959, Apr., v. 143, No. 3, 204–12.

Guineapigs were inoculated intramuscularly with lymphocytic choriomeningitis virus, and the subsequent distribution of virus in the body was determined by subinoculation of blood and organ material from animals killed at intervals after infection. Virus appeared in the blood on the 2nd day and in the brain on the 4th day. In animals infected similarly and given immune serum at the same time viraemia did not occur until the 3rd day, and the virus was present in the blood in lower titres; the appearance of virus in the central nervous system was also delayed by 2 days.

*D. J. Bauer*

WALLIS, R. C. *Culiseta melanura* **(Coquillett) and Eastern Equine Encephalitis in Connecticut.** *Mosquito News.* 1959, Sept., v. 19, No. 3, 157–8. [11 refs.]

"*Culiseta melanura* is a mosquito which has become of special interest since it is the only arthropod from which EEE virus has been repeatedly isolated. While circumstantial evidence has been reported indicating it may be a vector of the EEE virus either in endemic or epidemic cycles, the distribution of this species in Connecticut has not correlated with the distribution of farms where there has been virus activity. Studies

indicate that *C. melanura* will take blood from a wide range of hosts but is not persistent in its feeding activity."

SUDIA, W. D. & CHAMBERLAIN, R. W. **The Virus of St. Louis Encephalitis in Chickens.** *Amer. J. Hyg.* 1959, Sept., v. 70, No. 2, 197–207. [12 refs.]

A strain of St. Louis virus isolated from *Culex tarsalis* and after only 2 mouse-passages was used. 4 half-day-old chicks of 3 breeds were inoculated subcutaneously with 10,000 mouse LD50. In all viraemia was detected 48 hours (3·2–5·0 log mouse LD50) and 72 hours (3·0–4·7 log LD50) after infection. 10-fold dilutions of virus were then inoculated in the same way and the ID50 was found to be at least $10^{-8·5}$ for all 3 breeds. The ID50 for half-day-old chicks was found to be the same as the LD50 for 3-week-old mice. 10-week-old chickens were also highly susceptible, but less so than half-day-old chicks. *Culex pipiens*, infected by feeding on a chicken with a viraemia of $10^{-3·7}$, infected 63% of half-day chicks and 73% of 9-week chickens (only 45% of the latter circulated virus) by bite after a 14-day extrinsic incubation period. Half-day chicks had viraemia of $10^{-2·3}$ to $10^{-3·5}$ within the first 24 hours after inoculation, rising to a peak of up to $10^{-5·4}$ after 48–96 hours. Viraemia persisted for 5–7 days. In week-old chicks the viraemia was much lower and shorter and it further decreased in older birds. Maximum antibody titres were reached 1–3 months after infection or even later, and antibody persisted for at least 36 months. Attempts failed to demonstrate latent virus in the organs of birds 12 weeks after infection.

Mice infected with terminal dilutions of infected chicken blood often did not die of typical encephalitis within 10 days, but after the 10th day developed swelling of the abdomen and died between the 11th and 15th days. The caecum, stomach or small intestine was distended with an impacted mass. The explanation suggested is failure of persistalsis due to involvement of the autonomic nervous system.

These studies suggest that domestic chickens may be hosts of St. Louis virus for infections of man and may act as a link between wild birds and human beings. Chickens would make excellent sentinels for detection of St. Louis virus in an area and perhaps give warning of impending epidemics. The infection is completely symptomless in chickens, but antibody is formed and can be detected. *C. E. Gordon Smith*

OKUNO, T. **Isolation and Passage in One-Day Eggs of Japanese B. Encephalitis (JBE) Virus resulting in Attenuation of its Mouse Pathogenicity.** *Japanese J. Med. Sci. & Biol.* 1959, Apr., v. 12, Nos. 1/2, 71–8, 2 figs. [14 refs.]

The technique used was described by MATUMOTO [this *Bulletin*, 1958, v. 33, 1098]. Isolations were attempted in 1-day eggs and in mice from the brain of a fatal case of Japanese encephalitis, immediately after autopsy and after storing the brain for 4 months on dry ice. In the first attempt virus was isolated in mice but not in eggs, but at the second attempt both methods were successful. In the first passage 1 chick embryo died on the fourth day after inoculation and 1 mouse became paralysed on the 17th day. On passage in eggs, embryos died on the 2nd or 3rd days. In the 2nd passage in mice, they died in 5 days. 8th egg-passage virus was titrated in 1-day eggs and mice giving titres of 7·6 and 6·7 log LD50 per ml. respectively. A neutralization test in 1-day eggs showed that a Japanese encephalitis antiserum neutralized 2·8 log of the virus isolated. The 25th egg passage was passed another 26 times in 1-day eggs at limit dilution: the pathogenicity for eggs was unchanged by passage, but there was a gradual decrease in mouse-pathogenicity until there was a 5·3 log difference in titre in the 2 hosts. 18 similar passages with the Nakayama strain of Japanese encephalitis virus did not achieve a similar change. Mice dying of infection with the highly egg-adapted strain had incubation periods prolonged by 1–2 days compared with mouse-adapted virus and some paralysed mice survived for 2 weeks or even recovered, which never occurs with mouse-adapted virus. Even $10^8$ egg LD50 given intraperitoneally to mice failed to produce symptoms. It is suggested that this egg-adapted strain might be used for production of a live-virus vaccine. *C. E. Gordon Smith*

WU, C. J. & WU, S. N. **[Serological Study and Virus Isolation for B Type Encephalitis in Cattle]** *Acta Microbiologica Sinica.* 1959, May, v. 7, Nos. 1/2, 40–42. [In Chinese.]

The English summary appended to the paper is as follows:—

"Sixty-eight specimens of blood were collected from three sources: 36 from cattle in a highly endemic region, 8 from a low endemic region, while the rest were from slaughtered cattle in local abattoirs. Among these, 7 produced signs of encephalitis on first inoculation into white mice. But on second passage, only one, of which the portion of brain treated with mucin-broth could only reproduce the disease serially, while that portion of the same brain suspended in broth failed to produce any effect in mice.

"The same specimens of blood were examined for antibodies towards B type encephalitis by means of the complement fixation and neutralization tests. Sera from slaughtered cattle showed high percentages of neutralization, namely, 53%, whereas only 13% gave positive complement fixation. Sera from cattle from highly endemic regions showed 19% and 16% positives respectively; whereas those from calves in low endemic regions gave only positive complement fixation test but negative neutralization. From these, it was concluded that inapparent infection exists among cattle in Fukien Province."

WU, C. J., WU, S. N. & CHANG, H. G. **[On the Study of Encephalitis Virus isolated from Naturally Infected Chicken]** *Acta Microbiologica Sinica.* 1959, May, v. 7, Nos. 1/2, 43–7. [10 refs.] [In Chinese.]

The English summary appended to the paper is as follows:—

"During the epidemics of B type encephalitis in 1954

and 1955 in Fukien, an epizootic simultaneously occurred among chicken causing the loss of several hundred heads. From seven dead or dying birds, three strains of encephalitis virus were isolated from chicken brains, and identified to be B type encephalitis by the following tests: Hemagglutination test of a great variety of red blood cells; hemagglutination inhibition tests with serum prepared with Yakanawa strain; range of animal pathogenicity; cross neutralization and complement fixation tests with known B type encephalitis virus; and, finally, cross protection test in white mice. All the tests clearly indicated that the viruses isolated were not Newcastle Disease virus, but B type encephalitis indistinguishable from those isolated from human cases in the same localities.

"Attempt was made to isolated the virus from *Lashiohelea taiwana* captured from the chicken crops. However, probably owing to the early season, no positive results were obtained. But the possibility of chicken as a source of infection of B type encephalitis virus must now be considered in the control of this disease."

BULLOCK, H. R., MURDOCH, W. P., FOWLER, H. W. & BRAZZEL, H. R. **Notes on the Overwintering of *Culex tritaeniorhynchus* Giles in Japan.** *Mosquito News.* 1959, Sept., v. 19, No. 3, 184–8. [23 refs.]

"During the winter of 1957–1958, it was determined that *C. tritaeniorhynchus* overwinters as adults in Japan. The main habitats in which specimens were co lected were brush and wood piles of the common pine, *Pinus densiflora.* Specimens have also been collected from wood piles of *Zelkova serrata* and *Quercus acuta,* bundled bamboo, and from a cave. Data from pilot laboratory studies indicate that there is a possibility that *C. tritaeniorhynchus* does not require a blood meal to overwinter. If this be the case in nature, it would be unlikely that this species would be an overwintering host for virus unless transovarian transmission is involved."

NIR, Y. D. **Airborne West Nile Virus Infection.** *Amer. J. Trop. Med. & Hyg.* 1959, Sept., v. 8, No. 5, 537–9. [11 refs.]

"A clinical case of probable West Nile virus infection was associated with exposure to an infectious aerosol emanating from a badly-assembled Waring blendor containing infected material.

"A monkey, 12 mice and 6 hamsters were infected by exposure to an aerosol containing West Nile virus."

GRESÍKOVÁ-KOHÚTOVÁ, M. & ALBRECHT, P. **Experimental Pathogenicity of the Tick-Borne Encephalitis Virus for the Green Lizard, *Lacerta viridis* (Laurenti 1768).** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 258–63, 6 figs. (4 on 2 pls.)

*Ixodes ricinus*, the vector of Russian spring-summer group of encephalitis in Czechoslovakia, was found to be closely associated with the green lizard. Lizards were inoculated subcutaneously with mouse-brain virus of the Hypr strain after 51–53 mouse passages. Blood was collected at intervals from the orbital sinus and titrated, after pooling, by mouse inoculation.

Of 16 lizards infected, one showed lethargy on the 10th day and 2 others showed photophobia in addition. They developed ataxia and one of them had spastic paresis of the limbs together with extension and twisting of the head and opisthotonus. Viraemia was found from 6 hours to 10 days after infection. Virus was also isolated at titres of $10^{-1}$ to $10^{-2}$ from brain and other organs of the lizards showing symptoms. Of the lizards without symptoms, virus was recovered only from those killed on the 16th day after infection. In lizards with marked symptoms, focal necrosis of nerve cells and circulatory disturbances were seen in the brain. Pooled serum from 8 lizards, 6–7 weeks after infection, neutralized over 10,000 LD50 of virus.

*C. E. Gordon Smith*

BÁRDOS, V. & DANIELOVÁ, V. **The Tahyna Virus—a Virus isolated from Mosquitoes in Czechoslovakia.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 3, 264–76, 1 map & 1 fig. [17 refs.]

Attempts to isolate a neurotropic virus from mosquitoes were made because a large proportion of neuro-infections of man and horses in East Slovakia were unexplained. An area of marshy forest and pastures in a riverine area subject to spring floods was chosen. There were a number of villages engaged in cattle rearing in the area. Mosquitoes enter houses only when very numerous but enter cattle sheds freely.

Mosquitoes were caught (1) in forest and woods surrounding the pastures, (2) in cattle sheds and poultry houses. Mosquitoes caught outside were mainly unfed, but those in the cattle sheds were commonly freshly engorged. In June mosquitoes were caught mainly outside and 96% were *Aëdes sticticus.* In July 75% of mosquitoes caught were *Aëdes vexans* and were caught both outside and in cowsheds. In August 89% of the catch were *Aëdes vexans* which were taken mainly indoors. Mosquitoes were taken alive to the laboratory where they were immediately frozen at − 25°C. The frozen mosquitoes were, next day, identified and ground up in batches of 50. Antibiotics were added to the centrifuged material which was transported on ice to another laboratory. There the material frozen at − 35°C. and, next day, inoculated into suckling mice. Virus was isolated from 2 batches of *Aëdes caspius* and 3 of *Aëdes vexans.* All the positive pools were of mosquitoes caught in farm buildings in July and August. *Aëdes vexans* breeds in warm, shallow water in forest where it remains during the day. In the early evening it leaves the forest to bite mainly cattle and commonly enters cowsheds. *Aëdes caspius* breeds in flooded pastures and along the unshaded edge of forest. This species is strongly attracted by cattle with which it lives in close association and follows them into the cowsheds.

Re-isolations of the virus strains were successful. The incubation period in 2–3-day-old mice was 4–6 days reducing to 2–3 days with passage. The virus was pathogenic for suckling mice by subcutaneous inoculation and for adults by intracerebral inoculation. It was also pathogenic for hamsters and suckling white rats,

but not for guineapigs or rabbits. All 5 strains were shown to be identical by a neutralization test. The virus passed a Seitz filter and was inactivated by both sodium desoxycholate and ether. It was shown not to be lymphocytic choriomeningitis, ectromelia or Theiler's viruses, nor was it foot and mouth or vesicular stomatitis viruses. In cross-neutralization tests it was distinguished from Russian spring-summer, St. Louis, Rio Bravo [bat salivary gland virus, this *Bulletin*, 1957, v. 32, 216, 908], eastern and western equine, Sindbis, Semliki Forest and encephalomyocarditis viruses. Antibodies were found in man, horses, cattle and pigs, but not in calves, foals or poultry. *C. E. Gordon Smith*

Bugyaki, L., with the collaboration of J. H. M. Moons & S. R. Blockeel. La survie du virus fixe de Pasteur dans le vaccin antirabique phénique type Fermi-Semple et sa relation avec le degré d'immunité conférée. [**The Survival of Pasteur's Fixed Virus in Phenolized Anti-Rabies Vaccine of the Fermi-Semple Type and its Relation to the Degree of Immunity Conferred**] *Ann. Soc. Belge de Méd. Trop.* 1959, June, 30, v. 39, No. 3, 275–80.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 118.]

Hsu, H. L., Ni, E. L., Huang, H. C. & Chu, C. M. [**Comparative Studies on Rabies Vaccine prepared with Sheep, Rabbit and Mouse Brains**] *Acta Microbiologica Sinica.* 1959, May, v. 7, Nos. 1/2, 60–65. [In Chinese.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 117.]

Diercks, F. H. **Isolation of a Type 2 Dengue Virus by Use of Hamster Kidney Cell Cultures.** *Amer. J. Trop. Med. & Hyg.* 1959, July, v. 8, No. 4, 488–91, 1 fig.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 114.]

## IMMUNITY

Groot, H., Oya, A., Bernal, C. & Barreto-Reyes, P. **Guaroa Virus, a New Agent isolated in Colombia, South America.** *Amer. J. Trop. Med. & Hyg.* 1959, Sept., v. 8, No. 5, 604–9.

Guaroa is a new settlement in the Orinoco River basin at the edge of a large savannah and near a stretch of tropical rain forest. At the time of this investigation the population was about 200 including 50 soldiers and all had worked in the forest. Cases of severe fever was reported, but when the authors arrived no one was sick. Blood was taken, however, from 128 people and subsequently inoculated into mice 1–3 days old. 6 strains of virus were isolated and successfully re-isolated. Subsequent serum samples were obtained from 4 of these persons and neutralizing antibody demonstrated in them, but not in the specimens from which virus was isolated. A low-titre haemagglutinin was prepared from suckling mouse brain agglutinating at a *p*H range 5·7–6·2. One of the virus strains was compared with a wide variety of arboviruses and a relationship found only by haemagglutinin-inhibition with California encephalitis virus: California antiserum inhibited Guaroa antigen, but Guaroa antiserum did not inhibit California antigen. Complement-fixation tests did not reveal this relationship.

Guaroa virus readily passes a Seitz EK filter.

Suckling mice inoculated intracerebrally with the human serum died after 6–9 days; after passage the mice died after 3–5 days. Similarly inoculated adult mice (2nd and 3rd passages) died after 5–8 days. Titres in suckling mouse brain were $10^{-5\cdot0}$ to $10^{-6\cdot8}$ per 0·03 ml. Rhesus monkeys inoculated subcutaneously with the human serum were unaffected clinically, but circulated about 100 LD50 (mouse) per 0·03 ml. of serum. Of 2 rhesus monkeys inoculated intracerebrally, 1 developed marked spastic paralysis of the lower limbs 14 days after inoculation, but subsequently recovered. Guineapigs inoculated intracerebrally were unaffected.

The only evidence of the symptomatology of the infection in man is that one of the 6 people from whom virus was isolated had a mild fever. 4 others complained of no symptoms. 44% of 110 sera from Guaroa residents were found to have neutralizing antibody to the virus although none had been more than 10 months in the area. *C. E. Gordon Smith*

Burnet, M. **Auto-Immune Disease. I. Modern Immunological Concepts.** *Brit. Med. J.* 1959, Oct. 10, 645–50, 2 figs. [11 refs.] **II. Pathology of the Immune Response.** *Ibid.*, Oct. 17, 720–25, 4 figs.

The first paper is a brief presentation of the clonal selection theory of antibody production. This presupposes that individual mesenchymal cells are capable of a high mutation rate and produce genetically-determined specific globulins which can interact with specific antigens. In the adult animal the presence of an antigen stimulates the appropriate mesenchymal cell to proliferate and differentiate—those of the progeny which produce a particularly appropriate globulin will be selectively stimulated. *In utero* it is necessary to postulate that the occurrence of an antigen leads to degeneration and "forbidding" of the mesenchymal cells capable of producing the appropriate globulins. Thus "self" antigens cause elimination of the mesenchymal cell-clones capable of producing the corresponding globulins. These are described as "forbidden" clones. Foreign antigens introduced *in utero* or soon after birth may act as "self" antigens so that immunological tolerance develops.

The second paper discusses the application of the clonal selection theory to auto-immune disease. Certain

additional assumptions are required: some anomaly must occur in the control mechanism of mesenchymal cell populations to permit emergence of a "forbidden clone". Where the "self" antigen concerned is constantly and abundantly in contact with the mesenchymal cells, forbidden clones are unlikely to establish themselves and auto-antibodies to major plasma and body fluid components have not in fact been detected. If, however, the "self" antigen has only limited accessibility to the mesenchymal cells and there is a failure of the control mechanism, a forbidden clone producing auto-antibody may develop. For this to produce lesions more of the antigen must be formed or liberated so as to come in contact with the mesenchymal cells, otherwise the antibody production would be self-limited. Thus a vicious circle is necessary to build up sufficient auto-antibody to produce lesions. The application of this hypothesis to acquired haemolytic anaemia and to disseminated lupus erythematosus and other collagen diseases is discussed. *C. E. Gordon Smith*

HIRSCH, J. G. **Immunity to Infectious Diseases: Review of some Concepts of Metchnikoff.** *Bact. Reviews.* 1959, June, v. 23, No. 2, 48–60, 1 fig. [12 refs.]

This review is based on an address given before the Symposium on Interplay between Infectious Agents and Phagocytic Cells at the 59th annual meeting of the Society of American Bacteriologists held at St. Louis, Missouri, in May 1959. The author has re-examined the ideas of Metchnikoff—first presented 70 years ago—concerning the mechanisms of host resistance to bacteria against the background of present information. The most noticeable fact is how little fundamental knowledge has been gained during these years.

A short biographical profile is given including Metchnikoff's description of his experiments with the rose-thorns and the star-fish larvae—the experiment which was the foundation of all his subsequent work on the phagocyte theory. Then, in turn, with extracts from Metchnikoff's writings the following aspects are reviewed: the definition of immunity given by Metchnikoff and still applicable; the role of host immunity in determining whether pathogenic commensals will give rise or not to infection—the example of susceptibility of diabetics to *Staphylococcus aureus* infections; natural immunity and acquired immunity including both cellular and humoral mechanisms; and non-specific acquired immunity. The greatest amount of knowledge has been gained in one aspect of host mechanism—the antibodies, especially their formation, structure, and specificity—but as the author points out, this work must be viewed in proper perspective against the broad background of immunology.

The pattern of bacterial infection has changed from the epidemic to the endemic type. We know that host resistance can be lowered by diabetes, by steroid drugs, by stress, starvation, irradiation and often by unknown factors. The author considers that more knowledge is needed on genetic and environmental factors and on the mechanisms controlling micro-organisms in the host.

*Elizabeth M. Harper*

ALADJEM, F., JAROSS, R. W., PALDINO, Rita L. & LACKNER, J. A. **The Antigen-Antibody Reaction. III. Theoretical Considerations concerning the Formation, Location, and Curvature of the Antigen-Antibody Precipitation Zone in Agar Diffusion Plates, and a Method for the Determination of Diffusion Coefficients of Antigens and Antibodies.** *J. Immunology.* 1959, Sept., v. 83, No. 3, 221–31, 6 figs. [14 refs.]

"1. Some aspects of the antigen-antibody reaction in agar diffusion plates were studied.

"2. A method was developed that permits the prediction of whether a zone of precipitation will form for given initial amounts of antigen and antibody. Calculated values were found to agree with experimental observations.

"3. An expression was obtained for the relation between the location of the zone of precipitation between antigen and antibody reservoirs and the time required for the appearance of the zone. Calculated values were found to agree with experimental observations.

"4. The relationship between diffusion coefficients of antigen and antibody and the curvature of the zone of precipitation was determined.

"5. Theoretical derivations of expressions for the determination of diffusion coefficients of antigens and antibodies are presented. Diffusion coefficients of human serum albumin, bovine plasma albumin and chicken ovalbumin and homologous rabbit antibodies were determined. Values were found to be in reasonable agreement with diffusion coefficients of antigens and antibodies determined by other methods. The outstanding property of this method for the determination of diffusion coefficients is its experimental simplicity."

OGATA, T., TACHIBANA, T., SUZUKI, K. & SUZUKI, T. **Quantitative Studies on the Antigen-Antibody Reaction by the Monolayer Technique. II. Desorption Experiments.** *J. Immunology.* 1959, Oct., v. 83, No. 4, 397–404, 4 figs. [10 refs.]

GARVEY, Justine S. & CAMPBELL, D. H. **The *in vivo* Stability of Antibody.** *J. Exper. Med.* 1959, Sept. 1, v. 110, No. 3, 355–68, 5 figs. [12 refs.]

Previous work by the present authors had suggested that antibody may be stabilized at tissue sites (*Internat. Arch. Allergy and Applied Immunol.*, 1958, v. 12, 70). The purpose of the present study was to examine further the antibody which appeared to be bound to antigen or normal tissue components.

Bovine serum albumin or keyhole limpet haemocyanin or both together were used as antigens to immunize rabbits by a series of intravenous injections. When precipitin production had reached a high level, the animals were fed yeast cells labelled with $^{35}S$. The newly produced antibody, in common with other plasma proteins, was labelled with $^{35}S$ amino acids within a few hours. After a time, when the circulating antibody had declined, antigen was again injected. Serum samples were taken at intervals and the specific activity of antibody was measured in antigen-antibody precipitates.

The specific activity of antibody was measured during the period of decline of precipitin levels and during the

anamnestic response. Radioactivity and antibody nitrogen in the antigen-antibody precipitates at the point of maximum precipitation were determined, allowing the assignment of a specific activity to antibody as counts/minute/gamma of antibody N in 1 ml. serum.

It was found that the initial antibody appearing in the circulation after an antigenic stimulus had a higher specific activity than that circulating before the stimulus. The appearance of antibody with a high specific activity was shown to be a specific response to the injected antigen. It was also shown that antibody had a higher specific activity than other serum proteins but a fractionation of non-antibody protein was not carried out.

It was concluded that these results strongly suggest the persistence of antibody in the tissues and the mechanism of this persistence is discussed in relation to the persistence of antigen in liver tissue. *Max Sussman*

TAYLOR, A. B. & LEON, M. A. **Kinetics of Human Complement. IV. Kinetics of the Inactivation of the C'3 Complex by Hydrazine.** *J. Immunology.* 1959, Sept., v. 83, No. 3, 284–90, 5 figs. [21 refs.]

LEON, M. A., with the technical assistance of A. RANSBY. **V. Decay of the Intermediate Complex EAhuC'$_A$.** *Ibid.*, 291–6, 6 figs.

iv. "1. A serum factor involved in the terminal, cation-independent stage of immune hemolysis is inactivated by hydrazine.

"2. The reaction kinetics favor a bimolecular mechanism for the inactivation.

"3. The reaction exhibits no Ca++ or Mg++ requirements and the rate is independent of ionic strength.

"4. The activation energy has been determined and the effect of pH investigated.

"5. The evidence indicates that the hydrazine reacts in the form of uncharged, free base.

"6. The inactivating properties of certain other reagents have been noted and discussed."

v. "1. At least two different mechanisms are responsible for the decay of the complex EAhuC'$_A$.

"2. The increase in the rate of decay with increasing concentration of EAhuC'$_A$ follows a sigmoid curve.

"3. Exposure of a single batch of EA to successive cycles of formation and decay of intermediate complexes results in decreasing lytic susceptibility to C'3 until a minimum is reached. The behavior of whole human and guinea pig complement with these cells is described.

"4. A hypothesis is advanced to describe these results which postulates an equilibrium between decayed components of complement in the sensitized cell and fresh complement in solution."

YOUNG, F. E. & LEPOW, I. H. **Further Studies on the Effect of Ca++ on the First Component of Human Complement (C'1).** *J. Immunology.* 1959, Oct., v. 83, No. 4, 364–71, 2 figs. [11 refs]

TODD, E. W., PILLEMER, L. & LEPOW, I. H. **The Properdin System and Immunity. IX. Studies on the Purification of Human Properdin.** *J. Immunology.* 1959, Oct., v. 83, No. 4, 418–27, 1 fig. [16 refs.]

LEPOW, I. H., PILLEMER, L. SCHOENBERG, M. D., TODD, E. W. & WEDGWOOD, R. J. **The Properdin System and Immunity. X. Characterization of Partially Purified Human Properdin.** *J. Immunology.* 1959, Oct., v. 83, No. 4, 428–36, 4 figs. [43 refs.]

INGRAM, D. G., BARBER, H., MCLEAN, D. M., SOLTYS, M. A. & COOMBS, R. R. A. **The Conglutination Phenomenon. XII. Immuno-Conglutinin in Experimental Infections of Laboratory Animals.** *Immunology.* Oxford. 1959, July, v. 2, No. 3, 268–82, 8 figs. [11 refs.]

The conglutinin titres of rabbits, guineapigs and mice infected with a variety of bacteria, protozoa, rickettsiae and viruses were determined.

The results showed that after successful infection there is an initial fall in the conglutinin titre. The titres of conglutinin, antibody (neutralizing or haemolytic complement-fixing), and complement rise together but conglutinin is the first to fall on recovery.

Mild infections, *e.g. Listeria monocytogenes* applied to the rabbit conjunctiva, give low conglutinin titres compared with systemic infections.

The viral infections gave low conglutinin titres probably because the rabbit is a poor host for the viruses used: elevated conglutinin titres have been found in human poliomyelitis.

In rabbits infected with *Trypanosoma brucei* very high titres were rapidly acquired and sustained, whereas killed suspensions acted only as an antigenic stimulus and provoked very low titres.

In *Rickettsia burneti* infections of guineapigs the conglutinin titres showed 2 peaks at about 25 and 65 days after infection corresponding respectively to the phase II and phase I antigens of this organism.

In chronic *Salmonella typhimurium* infections of mice the titre remained high both in affected animals and symptomless carriers. In such chronic infections conglutinin may play a part in the increased phagocytosis and resistance to heterologous infections.

The diversity of organisms used suggests that a shared antigen is not responsible for the common post-infective conglutinin elevation. The results are consistent with the production of conglutinin in response to the animal's own complement fixed by antigen-antibody reactions.

*Stewart Fletcher*

NAUMANN, G. & WILDE, J. Veränderungen elektrophoretischer Eiweissspektren von Seren nach deren Absättigung mit Bakteriensuspensionen. **[The Influence of the Absorption with Bacteria on the Electrophoretic Distribution of Serum Proteins]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Apr., v. 117, No. 4, 325–40. [54 refs.]

By the methods of electrophoresis it is possible to subdivide the globulins and albumins already known and 18 separate fractions have already been recognized.

Discussion of the peculiarities of electrical change and motility which characterizes the albumin and globulin fractions respectively led to the conclusion that the gamma globulins are specially adapted to take part in the defence mechanisms of the body. In fact, the following antibodies have been found to be gamma

globulins:—typhoid and paratyphoid, brucella and streptococcal agglutinins, also the conglutinins appearing in mononucleosis, the antihyaluronidase which may appear in streptococcal infections, and some allergic antibodies. In syphilis, however, it has been observed that in the early stages the reagin is in the gamma globulin whereas later the specific reagins are more likely to be found with the beta globulin fraction. Observations on antibodies to pneumococci in horse sera, however, suggest an early stage in which the antibodies appear in a fraction between the beta and gamma globulins, but a later association with the gamma globulin.

In the case of antitoxic sera, diphtheria or tetanus, there is an early appearance in gamma globulin with a later move over to the more mobile T fraction, *i.e.* that between gamma and beta globulin mentioned above.

The authors' observations refer to the sera of immunized cats and also of human beings, both normal and immune to *Brucella abortus*.

Examinations of these both before and after removal of all antibody which could be detected by the usual immunological techniques showed a definite fall in gamma globulin content to have followed the removal of antibody and a more dubious fall in beta globulin. Similar results were obtained on saturating cat serum with staphylococcal suspension and the serum of a rabbit with *Proteus* suspension when it had been immunized with such material. Control observations on samples of serum exposed only to similar physical manipulations did not show any corresponding decrease of globulin. *J. W. McLeod*

LINZ, R. & MANDELBAUM, E. Phagocytose *in vitro* de bactéries par les leucocytes du Cobaye. Rapports quantitatifs. [*In vitro* **Phagocytosis of Bacteria by Guineapig Leucocytes. Quantitative Report**] *C.R. Soc. Biol.* 1959, v. 153, No. 6, 1079–82.

The authors studied the effect of the concentration of leucocytes and bacteria on *in vitro* phagocytosis. Suspensions of leucocytes in a physiological citrated solution, containing approximately 40,000 cells/ml. were diluted $^1/_5$ and $^1/_{25}$. 2 strains of bacteria were examined, *Escherichia coli* K.12 and Twort's strain of *Staphylococcus albus*. Suspensions of the former contained approximately $10^7$ bacteria/ml. and the latter $2 \times 10^7$ micrococci/ml.

0·05 ml. of undiluted suspension and of suspensions diluted $^1/_5$ and $^1/_{25}$ were mixed with 0·45 ml. of undiluted leucocyte suspension and of leucocyte suspension diluted with $^1/_5$ and $^1/_{25}$.

Tubes were incubated in a water bath at 38°C. for 20 minutes and centrifuged. Smears prepared from the deposit were stained by the May-Grunwald-Giemsa method. 500 leucocytes were examined on 2 smears from each mixture and the phagocytic index calculated (the average number of bacteria ingested per leucocyte).

At equal concentrations of leucocytes, the proportion which phagocytosed effectively increased when the concentration of bacteria was raised. At equal concentrations of bacteria, the proportion of leucocytes which phagocytosed effectively was greater at lower concentrations of leucocytes. When the average number of bacteria per leucocyte was 5,000 (*E. coli*) and 10,000 (*Staph. albus*) 100% of the leucocytes capable of phagocytosis were participating efficiently, and all contained bacteria. Some had at least 12. At lower concentrations of bacteria, some leucocytes contained a large number (50–100) but not all phagocytes had ingested bacteria.

*May F. McCallum*

# Book Review

UNITED KINGDOM: **History of the Second World War. The Army Medical Services. Campaigns. Vol. III. Sicily, Italy, Greece (1944–45)** [CREW, F. A. E. (F.R.S.)]. pp. xxxviii+645, numerous illustrations. 1959. London: H.M. Stationery Office. [£5.]

This volume of the medical history of the war deals with army medical services during the campaigns in Sicily, Italy and Greece (1944–45). It therefore covers the period from the planning stage for landings that took place in July 1943 to the end of the war in Europe. The environment in which the campaigns took place was far less healthy than that of the North African desert: the problems of malaria, typhus, intestinal infections, venereal disease, exposure to cold and wet, battle exhaustion from the strain of prolonged static warfare, and large disorganized civil populations were all encountered in acute form. At the same time the army medical services worked up to their peak of efficiency, and in these campaigns—not remote from the United Kingdom and the U.S.A.—had at their disposal ample if not unlimited supplies of newly invented agents for prevention and cure never before available in military (or for that matter, civil) history. Of these, penicillin and DDT were outstanding; penicillin revolutionized the treatment of venereal diseases, and the reputation of DDT was established at the highest level when, by its use, the Naples typhus outbreak was stopped abruptly.

Military operations throughout are described in detail and, judging by the index, two-thirds of which is devoted to the names of medical units, it should be possible to find in the book the location of any unit on almost any day. Is this important enough to justify the size of the volume, 14–16 years after the events described? It appears to be the main theme of the book: the actual organization and reorganization of medical services in the light of experience and changing conditions, which might be its chief interest, is dealt with piecemeal and

is secondary to the accounts of operations themselves. Though the narrative is of sustained interest throughout, any enquirer into medical organization in wartime, seeking information on this period of unprecedented efficiency, is faced with a great deal of extraneous reading. The general index could have been fuller and more helpful. If the need should arise to review the lessons taught by past experience and apply them to future campaigns, there may be little leisure for prolonged reading at the relevant time. However, the book never lacks interest and, granted the necessary leisure, makes excellent reading. The sections on specific diseases, notably malaria, are valuable and often enthralling records of achievement, though the quelling of the Naples typhus outbreak, a milestone in medical history, is described all too briefly and modestly.

*B. A. Waddy*

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